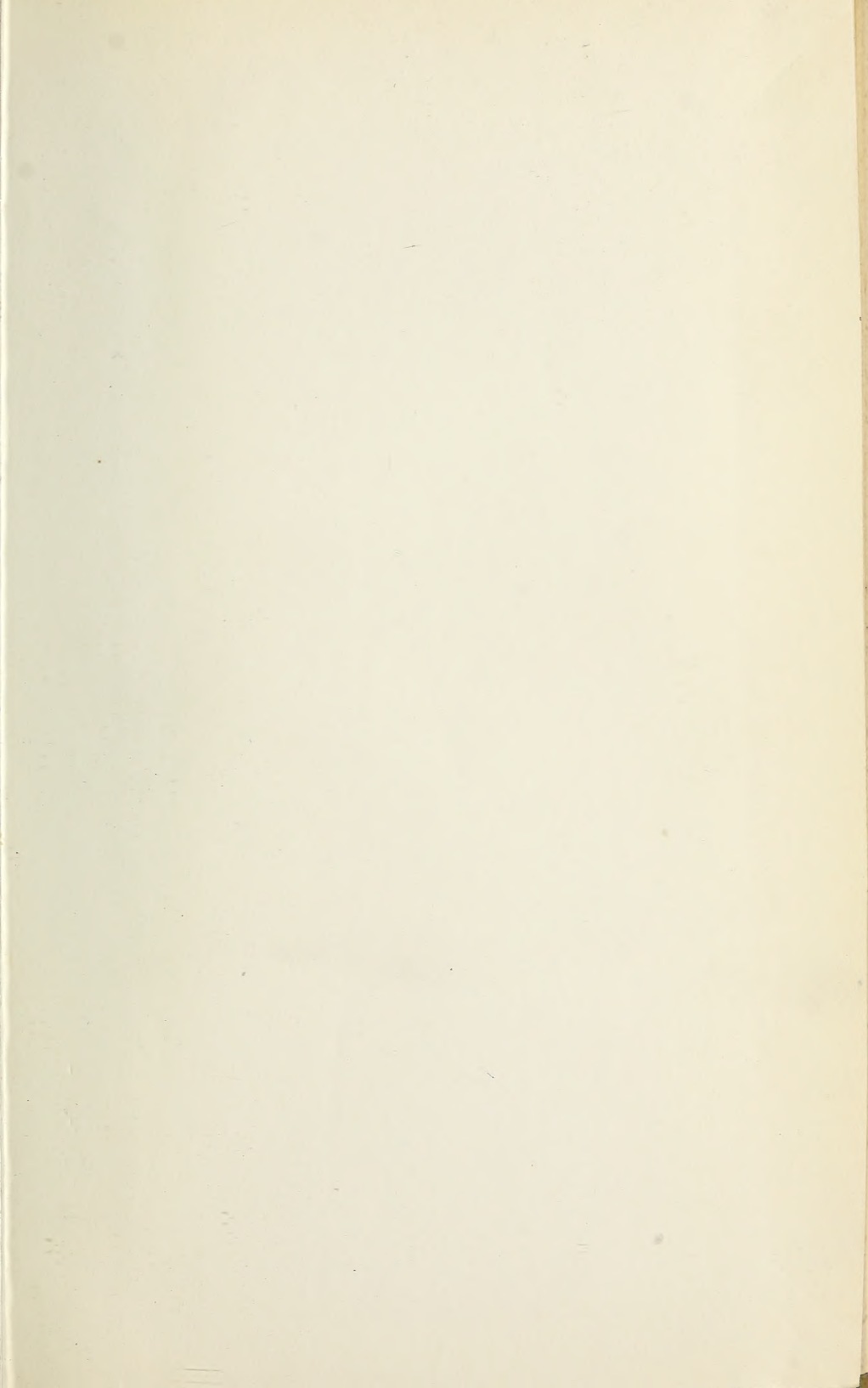


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Public Health and Marine-Hospital Service of the United States

HYGIENIC LABORATORY.—BULLETIN No. 47

OCTOBER, 1908

STUDIES ON THYROID

I.—THE RELATION OF IODINE TO THE PHYSIOLOGICAL ACTIVITY OF THYROID PREPARATIONS

By

REID HUNT

and

ATHERTON SEIDELL



A page from a manuscript, likely a liturgical book, featuring musical notation on staves. The notation consists of square neumes written on four-line red staves. The text is written in a Gothic script, with some words in red ink (rubrics). The page is numbered '1' in the top left corner. The text appears to be a portion of a Mass, possibly the Introit or Kyrie, given the presence of 'Kyrie' and 'Kyrie eleison'.

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SYNOPSIS AND TABLE OF CONTENTS.

	Page.
INTRODUCTION.....	7
Value of thyroid as a drug. Importance of a knowledge of the relation between the physiological activity and the iodine content. Older views on the relation of iodine to the thyroid. Baumann's discovery of iodine in the thyroid. Conflicting views as to the significance of the iodine.	
PART I. THE PARALLELISM BETWEEN THE PHYSIOLOGICAL ACTIVITY AND THE IODINE CONTENT OF THYROID.	
A. <i>Historical</i>	11
Review and discussion of the principal views on this subject. The chief objections which have been made to Baumann's view that iodine is an important, not an accidental, constituent of the thyroid. The experimental work bearing directly upon the problem. Lack of satisfactory methods.	
B. <i>Experimental</i>	19
Methods, effect of feeding thyroid upon the susceptibility of animals to various poisons. Advantages of the method.	
1. Experiments with acetonitrile.....	21
Theory of the physiological action of acetonitrile. Effect of acetonitrile upon sulphur metabolism.	
a. Experiments on mice.....	22
<i>Preliminary experiments and theoretical considerations.</i> —The feeding of thyroid increases the resistance of mice to acetonitrile. Experiments showing what large amounts of the poison may be neutralized by very small amounts of thyroid. Delicacy of the method for detecting minute amounts of thyroid mixed with other substances.	
<i>Conditions influencing the resistance of mice to acetonitrile.</i> —Variations in the resistance of different groups of mice to the poison. Influence of season, diet, etc.	
<i>On the manner in which thyroid influences the resistance of mice to acetonitrile.</i> —Not a simple chemical interaction between the thyroid and the poison. Bearing of these experiments upon the theory of the detoxicatory function of the thyroid.	
i. Experiments with "iodine free" thyroid.....	32
Conception of "iodine free" thyroid. Conflicting views as to the activity of such thyroid. Experimental. Differences in activity between different preparations of "iodine free" thyroids. General conclusions.	
ii. Experiments with commercial sheep thyroids.....	50
Relation of dose to physiological effect. Outline of methods. Experimental. Parallelism between iodine content and physiological activity.	
iii. Experiments with thyroids from various animals...	71

PART I. THE PARALLELISM BETWEEN THE PHYSIOLOGICAL ACTIVITY AND THE IODINE CONTENT OF THYROID—Continued.

B. *Experimental*—Continued.

Methods, effect of feeding thyroid upon the susceptibility of animals to various poisons. Advantages of the method—Continued.

1. Experiments with acetonitrile—Continued.	Page.
<i>b.</i> Experiments on rats.....	72
Thyroid lowers the resistance of rats to acetonitrile.	
Parallelism between the iodine content and the physiological activity. General conclusions.	
2. Experiments with morphine.....	77
Introduction. Resistance of rats, mice, and guinea pigs to morphine diminished by feeding of thyroid.	
<i>a.</i> Experiments on white rats.....	78
Parallelism between physiological activity and iodine content of thyroid preparations.	
<i>b.</i> Experiments on mice.....	85
<i>c.</i> Experiments on guinea pigs.....	87
<i>Conclusions from the experiments with morphine</i>	90
Explanation of effects of thyroid upon resistance to morphine. Possible clinical bearings.	

PART II. ON THE NATURE OF THE RELATION BETWEEN THE IODINE PERCENTAGE AND THE PHYSIOLOGICAL ACTIVITY OF THYROID..... 93

Historical: Roos's experiments on the activity of thyroid the iodine content of which was increased by the administration of potassium iodide. Discussion of Roos's results.

Experimental demonstration that the activity of thyroid iodized *in vivo* is increased in proportion to the increased iodine content.

1. Experiments with acetonitrile—	
<i>a.</i> Experiments on mice.....	95, 110
<i>b.</i> Experiments on rats.....	103
2. Experiments with morphine—	
<i>a.</i> Experiments on mice.....	106
<i>b.</i> Experiments on rats.....	107
Bearing of the results on the question whether there is a casual relation between the iodine content and the physiological activity.	

STUDIES ON THYROID: I. THE RELATION OF IODINE TO THE PHYSIOLOGICAL ACTIVITY OF THYROID PREPARATIONS.

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INTRODUCTION.

Thyroid is a unique drug and occupies a place in therapeutics which can not be filled, even imperfectly, by any other known therapeutic agent. Its use was the first practical application of the doctrine of internal secretion and it still remains the most striking example of the conscious utilization, for therapeutic purposes, of an "hormone."

Although much has been learned in recent years in regard to the function of the thyroid as a glandular organ and also as to the effects of the administration of thyroid preparations upon the organism, both in health and in disease, little progress has been made in the study of thyroid as a drug. The "active principle" of the gland is unknown, and there are no generally accepted means, aside from actual clinical tests, of determining the relative value of different thyroid preparations.

A very important advance in our knowledge of thyroid as a drug was made when Baumann^a discovered in 1895 that the gland usually contains iodine. Since that time the chief interest in the chemistry of the thyroid has centered around this iodine, but the opinions as to the physiological significance of the latter are as far apart to-day as they were twelve or thirteen years ago.

The question of the relation of the iodine to the physiological activity of thyroid is from the pharmacological standpoint the most important problem connected with this drug; this is the subject of the present bulletin.

^a E. Baumann, *Ztschr. f. physiol. chem.*, Strassb., 1895-96, **21**, p. 319.

Before considering the main problem, however, a few words may be devoted to certain phases of the older history of the thyroid. The relation of iodine to this gland had been for many years a matter of interest to physicians and was much discussed even before Baumann's important discovery. It has long been recognized that iodine has some special relation to the thyroid. Seven years after the discovery of the element iodine by Courtois, in 1812, Straub, of Berne, suggested that it was the active principle of the "toasted sponges" (*Spongia "usta" or "tosta"*) and the "*Aethiops vegetabilis*," which had been used in the treatment of goiter at least since the thirteenth century.^a Since 1820 iodine, as such or in combination, has been in constant use in the treatment of diseases of the thyroid.

About the middle of the last century great interest was aroused by the work of Chatin, Marchand, and others on the relation of iodine in drinking water to goiter. The more recent history of this subject began with the revival of interest in the physiology and pathology of the thyroid gland which was stimulated by the work of Gull and Ord on myxoedema and of Kocher and Reverdin on the effects of the removal of the thyroid in man. This work was followed, partly as a result of the stimulus of Brown-Sequard's ideas concerning internal secretion, by the introduction of organotherapy in the treatment of diseases of the thyroid. The brilliant results of this form of treatment led to the search for an "active principle," and this work culminated in the discovery of iodine in the thyroid by Baumann. In the year of Baumann's discovery Kocher,^b who had been much impressed by the similarity of the effects of iodine and thyroid in the treatment of goiter, had suggested the desirability of examining the thyroid for iodine; the tests made in Berne were, however, negative.

Baumann at first considered the iodine containing substance which he isolated and called iodothyrene to be the active principle of the thyroid; although he recognized later that in the gland much of this iodothyrene is in combination with proteins, neither he nor his co-workers seemed to have entertained any doubt that the iodine was very important for the physiological activity of the thyroid.

Following Baumann's discovery, determinations of the amount of iodine were made in the thyroid in a great variety of conditions; the influence of health, disease, sex, pregnancy, age, locality (near or remote from the sea, on the plains, and in the mountains), diet, climate, etc., was investigated. The amount of iodine in the thyroids of a great variety of animals was also determined. Far-reaching conclusions were drawn from such studies, especially as regards the relation of iodine to the diseases of the thyroid itself (various forms of

^a cf. E. Harnack, München. med. Wchnschr., 1896, **43**, p. 196; G. Monéry, Fonction iodée de la glande thyroïde, Thesis, Lyons, 1903; Th. Kocher, Die Therapie des Kropfes, Deutsche Klinik, Berl. and Wien, 1905, **8**, p. 1115.

^b Th. Kocher, Cor. Bl. f. schweiz. Aerzte, 1895, **25**, p. 3.

goiter) and to various forms of insanity. A vast number of data were collected, but these were often contradictory and not easily correlated.

The result was that within a few months after Baumann's first publication on the subject objections began to be urged against the view that the iodine is an important constituent of the thyroid. These objections have been repeated and still others urged up to the present time; they will be considered in detail in the following pages.

Part I.

THE PARALLELISM BETWEEN THE PHYSIOLOGICAL ACTIVITY AND THE IODINE CONTENTS OF THYROID.

A. HISTORICAL.

The views as to the relation of the iodine to the physiological activity of the thyroid may be classified under three heads: (1) Some investigators hold that the activity of thyroid is directly proportional to and dependent upon its iodine content and that thyroid free of iodine has no physiological activity. (2) There is another group of writers who take the view that there is no relation between the physiological activity of thyroid and its iodine content and that no importance should be attached to the iodine which is usually present in the thyroid. (3) Other writers admit that there is a parallelism between the physiological activity and the iodine content, but deny that the former is dependent upon the latter. Some of those holding this view apparently consider that the iodine is simply associated with the active part of the gland in some unknown, perhaps accidental, way. Others hold that the larger amount of iodine in active thyroid results from the activity of the gland itself; they consider that the more active the gland the larger the amount of iodine it is able to hold in combination. This latter view is closely connected with the theory that one of the functions of the thyroid is to take up injurious substances (including iodine) and to render them harmless.

Some of these theories have been combined. Thus von Cyon supposes the thyroid to take up iodine, by which process the latter is rendered harmless and at the same time a new compound, useful as an internal secretion, is formed.

We believe that these conflicting views have resulted partly from the failure of previous writers to recognize that thyroid free of iodine has a certain degree of physiological activity and partly from the fact that there has been a confusion of several distinct problems and that authors have often looked upon the subject from but a single point of view.

Baumann and some of the other earlier workers in this field apparently entertained no doubts as to the iodine being an important part of the "active principle" of the thyroid. They based this view upon the physiological action of iodothyrene in health and disease ^a and

^aE. Baumann and E. Roos, *Ztschr. f. physiol. Chem.*, Strassb., 1895-6, **21**, p. 487.

on the fact that iodine is so generally found in the thyroid in health and is apparently absent or present in diminished amounts in certain forms of goiter.

Before discussing in detail the chief arguments in favor of Baumann's view certain of the objections which have been made to it may be considered. The principle of these objections may be classified as follows:

a. Iodine is not invariably found in the thyroids of healthy animals; when it does occur there are great variations in its amount.

b. Artificially iodized proteins, including those of the thyroid itself, are inactive physiologically or the activity is not at all proportional to the amount of iodine which has been added; this is also true of iodothyrene to which iodine has been added *in vitro*.

c. Thymus was reported to be of value in the treatment of goiter.

d. The reputed "active principle" of the thyroid (Baumann's iodothyrene) did not prevent tetany in animals from which the thyroids had been removed.

e. Efficiency of iodine compounds other than iodothyrene in goiter.

These points may now be considered in more detail:

a. *Iodine is not invariably present in the thyroid.*—Miwa and Stoeltzner^a early laid great emphasis on this point. They argued that if the theory that iodine is an essential constituent of the thyroid is correct, then the absence of iodine in the thyroid of an individual would have the same serious effects as the absence of the gland itself. They pointed out that Baumann had reported the frequent absence of iodine from the thyroid of children, and of dogs fed on meat; yet neither the children nor the dogs had shown any indications of thyroid insufficiency. Miwa and Stoeltzner confirmed Baumann's observations on the frequent absence of iodine from the thyroids of children; they also stated that the hen's egg contains no iodine and that the young chick thus begins life without iodine. They emphasized the dependence of the iodine content of the thyroid upon the diet. From these facts Miwa and Stoeltzner argued that the iodine usually found in the thyroid has no more significance than the traces of copper so often found in the liver. Similar arguments were advanced with great emphasis by Neumeister^b at about the same time; he stated that the iodine of the thyroid has absolutely no physiological significance.

These arguments of Miwa and Stoeltzner and of Neumeister have been repeated to the present time; the facts upon which they were based have received abundant confirmation.^c Thus Töpfer in Vienna

^a S. Miwa and W. Stoeltzner, *Jahrb. f. Kinderh.*, 1897, **45**, p. 83.

^b R. Neumeister, *Lehrbuch der physiologischen Chemie*, 2d ed., 1897, p. 520. Cf. also Halliburton in Schäfer's *Textbook of Physiology*, 1898, **1**, p. 89.

^c An abstract of the literature showing how frequently iodine is absent from the thyroids of infants is given on page 33 of this bulletin.

found no iodine in the thyroids of cattle.^a Roos^b found no iodine in the thyroids of three foxes; none in that of a polecat; none in that of a wild cat; he found it in but two of six martens; it was absent from the thyroids of four domestic cats and present in but traces, or in very small amounts, in those of five others; it was absent in four of eleven dogs, in two of four horses, and three of seven hogs.

In many cases the presence or absence of iodine is dependent upon the character of the food which the animal has received.

The thyroids of herbivorous animals, whose food usually contains small amounts of iodine, are almost always richer in this element than are those of carnivorous animals, whose food is usually poor in iodine.^c Sheep pastured near the sea may have double the amount of iodine in their thyroid as those pastured in inland regions.^d The amount of iodine in the thyroid of omnivorous animals (hog, dog, man) is especially variable. Nagel and Roos^e found the percentage in the dried glands of hogs to vary from 0 to 0.075, although the glands were obtained from the same slaughterhouse.^f Baumann found the percentage of iodine in the thyroid of horses to vary from 0.06 to 0.17.^g

As a rule it is not possible to detect any difference between the animals which have a large percentage of iodine in their thyroids and those which contain none or only traces: removal of the gland is followed by as severe symptoms in the latter as in the former. Thyroid free of iodine seems to meet the needs of the body as well as the thyroid that contains iodine.^h

Human thyroids also contain quite variable amounts of iodine, as was first pointed out by Baumann.ⁱ Jolin^j has recently summarized the entire literature on the occurrence of iodine in the thyroid of man and has reported a very large number of analyses of such thyroids obtained in Sweden; he found great variations in the percentage of iodine and was unable to discover any constant relation between its presence or amount and conditions of health or disease. He asks, "Can not the great variations in the iodine content of not only pathologically altered thyroids but also of normal glands, and especially the fact that thyroids may be found in adults as well as in children which contain no iodine or scarcely traces of it, simply depend upon the fact that the iodine is an accidental constituent

^a Töpfer, Wien. klin. Wchnschr., 1896, **9**, p. 141.

^b E. Roos, Ztschr. f. physiol. Chem., Strassb., 1899, **28**, p. 55.

^c E. Roos, l. c.

^d Th. Suiffet, J. de pharm. et chim., Par., 1900, [6] **12**, p. 50.

^e W. G. Nagel and E. Roos, Arch. f. (Anat. und) Physiol., Suppl.-Bd., 1902, p. 267.

^f A specimen of hog thyroid examined by us contained 0.33 per cent iodine.

^g Baumann, Ztschr. f. physiol. Chemie, Strassb., 1896, **22**, p. 17.

^h Exceptions to this will be referred to later.

ⁱ E. Baumann, Ztschr. f. physiol. Chem., Strassb., 1896, **22**, p. 1.

^j S. Jolin, Festschrift, O. Hammarsten, Upsala, 1906.

(nebensächlicher Bestandteil) of the thyroid and its secretion?" He further states that the fact that in the body iodine is found chiefly in the thyroid "does not prove that the iodine is necessary for the activity of this gland; it may be explained by supposing that the thyroid has, among other functions, that of taking up an excess of iodine in the blood and storing it."

Several other recent writers have expressed somewhat similar views.^a This point of view is, however, by no means new; Roos^b referred to it in 1899 in the following words:

To consider the accumulation of iodine in the thyroid as an accidental process which has no greater significance for the body than the storing up of certain metals in the liver seems to me to be a very unsatisfactory conception: for on it it is entirely unintelligible why the thyroid should use the iodine for the making of a substance (iodothyrene) which has such a marked effect upon metabolism and myxoedema instead of combining it in a much less active form, as occurs when iodine is allowed to react with proteins outside of the body.

Such studies as the above (they may be called statistical studies) have undoubtedly brought to light many facts, some of which are difficult to satisfactorily explain. Still they do not seem to us to weaken the conclusion that iodine is an important constituent of the thyroid. All the writers who have discussed this subject seem to have taken one of two extreme views—that iodine is necessary to any physiological activity, or that it has no part at all in rendering the thyroid active. No one seems to have suggested an intermediate view, viz, that thyroid free of iodine may have a certain degree of activity, although this is much less than that of thyroid containing iodine, until one of the present writers discovered that it is distinctly active in altering the resistance of animals to certain poisons.^c This subject will be discussed in detail in the experimental part of this section. It will suffice for the present to state that we believe this conception and the conclusions that may be drawn from it go far toward answering the arguments for the unimportance of iodine which have been drawn from statistical studies.

b. Physiological inactivity of artificially iodized proteins and colloid.—The question of the relation of the iodine to the activity of the thyroid was approached experimentally by Hutchinson,^d who prepared an artificial iodized nucleo-albumin from the thymus of calves. Samples of it contained from 4 to 7 per cent of iodine; it had no effect in myxoedema or upon the pulse, temperature, or weight of subjects to whom it was administered. Hellin^e had previously found iodized

^a Bunge, *Lehrbuch der Physiol. des Mensch.*, 2d ed., 1905, **2**, p. 631; S. J. Meltzer, *N. Yorker med. Monatschr.*, 1907, **19**, p. 223; Abderhalden, *Lehrbuch der physiol. Chem.*, 1907, p. 647.

^b E. Roos, *Ztschr. f. physiol. Chem.*, Strassb., 1899, **28**, p. 59.

^c R. Hunt, *J. Am. M. Ass.*, 1907, **49**, p. 1325.

^d R. Hutchinson, *J. Physiol.*, 1898-99, **23**, p. 181.

^e D. Hellin, *Arch. f. exper. Path. u. Pharmakol.*, Leipzig, 1897, **40**, p. 121.

albumin and nucleo-albumin prepared from the spleen to be inactive. Blum^a had also found iodized albumin almost without effect upon metabolism. Hutchinson also increased artificially the percentage of iodine in colloid derived from the thyroid. Although such a product contained nearly ten times as much iodine as the original material, it had no greater physiological activity. Hutchinson drew the following conclusions from these results:

One would conclude from the whole evidence that the iodine in the thyroid gland, if it plays an essential part in the activity of the latter at all, does so simply in virtue of the special form of combination in which it is present.^b

Hutchinson had apparently concluded from earlier work that not much importance was to be attached to iodine as a factor in determining the activity of the thyroid. Thus in 1896 he wrote as follows:^c

It must not * * * be supposed * * * that the iodine is necessarily the essential factor in the activity of the thyroid gland. One has only to realize the small proportion in which it is normally present—only a few milligrams in a whole gland—to be convinced of that. * * * Baumann has himself failed to find any iodine at all in the thyroid of some children. Yet I suppose such a gland is none the less active.

Blum^d and Roos^e had also early pointed out that thyroid proteins or iodothyrene to which iodine had been added *in vitro* were physiologically inactive or less active than the natural products containing much less iodine. Blum used this observation as an argument against the view that the iodine is a factor in the physiological activity (or "toxicity," as Blum denies that the thyroid produces an internal secretion) of the proteins of the thyroid; he applied this view also to the iodine which has been taken up by the living gland, maintaining that the iodization *in vivo* is strictly analogous to that *in vitro*. Roos^f endeavored to disprove Blum's theory by feeding iodine to dogs until the iodine content of the thyroid had been considerably increased; he stated that such thyroids showed increased physiological activity. Blum^g points out that Roos's figures are hardly conclusive in this respect. We have recently studied this phase of the subject, using new methods for determining the activity of the thyroid, and have completely confirmed Roos's results. (See Part II of this bulletin.)

c. *The value of thymus in goiter*.—Further arguments against the view that the iodine is an important constituent of thyroid have been based upon the statements that thymus has an effect in goiter similar

^a F. Blum, München. med. Wehnschr., 1898, **45**, p. 270.

^b Similar views have been expressed by G. Reinbach, Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1898, **3**, p. 309, and L. B. Mendel, Am. J. Physiol., Bost., 1900, **3**, p. 290.

^c R. Hutchinson, J. Physiol., 1896, **20**, p. 494.

^d F. Blum, München. med. Wehnschr., 1898, **45**, p. 335.

^e E. Roos, Ztschr. f. physiol. Chem., Strassb., 1898, **25**, p. 242.

^f E. Roos, Ztschr. f. physiol. Chem., Strassb., 1899, **28**, p. 40.

^g F. Blum, Verhandl. des Kong. f. inn. Med., 1906, **23**, p. 196.

to that of thyroid.^a Since most writers have found either no iodine in the thymus or only traces (in which case it was usually attributed to admixture with thyroid^b) the conclusion has been drawn that thymus free of iodine has a physiological effect similar to that of thyroid. In reply to this it may be stated that later writers seem to be agreed that thymus has very little activity in goiter. Even granting that thymus does possess a certain degree of activity of a character similar to that of the thyroid, this would not prove that iodine is not a very important constituent of the thyroid. One of the present writers^c recently showed that there is present in several organs of the body a substance or substances having a physiological action similar, at least in some respects, to that of thyroid, but that the latter, apparently on account of its iodine content, is far more active.

d. Inefficiency of iodothyryne in tetany.—Another argument against the view that the iodine-containing substance (iodothyryne) obtained from the thyroid by Baumann is the active constituent of the thyroid was that it did not prevent tetany in thyroidectomized animals.^d These experiments were performed before the importance of the parathyroids was recognized and the investigators were endeavoring to control symptoms with which the thyroid had little or nothing to do.

e. Efficiency of iodine compounds other than iodothyryne in goiter.—Baumann argued that iodothyryne was the active principle of the thyroid from the fact that its administration produced the same effects upon certain forms of goiter as did that of the thyroid itself. But attention was called to the fact^e that a great variety of iodine compounds, both inorganic and organic, had a similar effect in these conditions. Evidently, however, such arguments do not bear directly upon the question whether the iodine is of importance to the thyroid. Recent work indicates that these different forms of iodine are efficient simply because the iodine has a special affinity for the thyroid. The effect of iodine in the treatment of goiter is in reality an argument in favor of the view of the importance of iodine in the thyroid.

A very little consideration suffices to show that none of the above arguments have any very direct bearing upon the problem with which

^a J. Mikulicz, Berl. klin. Wehnschr., 1895, **32**, p. 342; G. Reinbach, Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1898, **3**, p. 309; R. H. Cunningham, J. Exper. Med., N. Y., 1896, **3**, p. 227.

^b E. Baumann, München. med. Wehnschr., 1896, **43**, p. 311; R. H. Cunningham, l. c.; H. G. Wells, J. Am. M. Ass., Chicago, 1897, **29**, p. 1009; L. B. Mendel, Am. J. Physiol., Boston, 1900, **3**, p. 285.

^c R. Hunt, J. Am. M. Ass., Chicago, 1907, **49**, p. 1325.

^d cf. G. von Bunge, Lehrbuch der Physiologie des Menschen, 2 ed., 1905, **2**, p. 632; E. Roos, Ztschr. f. physiol. Chem., Strassb., 1899, **28**, p. 41; 1899, **27**, p. 37.

^e cf. Von Bunge, l. c.

we are concerned, viz, the use of thyroid as a drug. It is not the condition of the thyroid in a living animal which is of interest in this connection. There may be and probably are delicate mechanisms by which the amount and strength of the secretion given off by the thyroid is accurately adjusted to the needs of the body. A gland may be supposed to form a large amount of very active material, but this may not reach the circulation owing to some abnormalities in the blood or lymph vessels or possibly to the absence of some stimulus which normally causes the secretion of the material. In the body the thyroid which has undergone cystic degeneration may be very ineffective in preserving health; but removed from the body and administered as a drug it may have pronounced effects. Similarly we may suppose that in some cases of Grave's disease the thyroid contains normal amounts of active material but that the conditions for the rapid secretion or for the reabsorption of the iodine are so favorable, or that the capacity of the organism to destroy the secretion is lowered, so that there is an accumulation of the active material in the body outside of the thyroid. In such a case there might be a condition of hyperthyroidism, but the gland when administered to an animal as a drug might not be very active. In other words, the effects of a dead organ when administered as a drug can not be compared with the activities of the living organ in the body. Many of the writers who have discussed the relation of iodine to the thyroid have confused these two distinct problems.

If we now turn to the experiments in which the question of the relation of iodine to the thyroid when used as a drug has been approached directly, we find that there is no difference of opinion: all who have worked upon the problem from this standpoint agree as to the importance of the iodine. Unfortunately, however, the experiments of this character are very few and the results are not quantitative.

The experiments bearing on this phase of the subject may be divided into three groups—(a) those in which the action of the thyroid upon metabolism, (b) upon different forms of goiter, and (c) upon the circulation was investigated.

The most important work upon the relation between the iodine content of the thyroid and its effects upon metabolism was done by Roos,^a who recorded the results of three such experiments upon a dog. In the first experiment the administration of 5 grams of desiccated children's thyroid containing 0.025 per cent iodine had almost no effect upon the excretion of nitrogen or upon body weight; later the administration of 5 grams of children's thyroid containing 0.18 per cent iodine caused an increase in the excretion of nitrogen of about 10 per cent. In the second experiment also a greater effect

^a E. Roos, *Ztschr. f. physiol. Chem.*, 1899, 28, p. 40.

was produced by the administration of the thyroid containing the larger percentage of iodine. In the third experiment, in which the dried thyroids of dogs were administered, 5 grams of a preparation containing no iodine had no effect, whereas 5 grams of a preparation which contained 0.35 per cent iodine was followed by a distinct increase in the nitrogen excretion and a slight loss of weight.

Roos's experiments were very few in number and the results not very striking, and perhaps do not justify the very positive conclusions he drew from them.^a Still they point very distinctly to the conclusion that thyroid rich in iodine has a more marked effect upon nitrogen metabolism than does thyroid poor in, or free of, iodine.

Roos also describes the effects of desiccated hog thyroids containing different percentages of iodine upon four cases of parenchymatous goiter. In all cases thyroid free of iodine had a very slight or doubtful effect, whereas thyroid containing iodine had a marked action in reducing the size of the goiter. In one case the use of doses of 0.5 gram thyroid containing 0.008 per cent iodine had a distinct effect, but the effect of the administration of equal doses of a thyroid containing 0.08 per cent iodine was more marked.

Roos himself recognized that only an approximate estimation of the quantitative effects of thyroid was possible either in metabolism experiments or in the treatment of goiter. He also pointed out the difficulties of drawing any conclusions from observations upon thyroid-ectomized animals, and stated that he deemed it useless to try this method.

Oswald tested the activity of thyreoglobulin containing little iodine upon metabolism, and von Cyon investigated its effects upon the irritability of the vagi.^b In the two experiments upon metabolism reported by Oswald the thyreoglobulin poor in iodine produced no effect in one case and very slight, if any, in the other; thyreoglobulin rich in iodine produced a marked increase in the nitrogen excretion. Von Cyon reported that thyreoglobulin obtained from colloid goiters and which contained 0.19 per cent iodine had a distinct effect upon the irritability of the vagi, but that this was less than that produced by normal thyroid with a higher percentage of iodine. Von Cyon and Oswald^c had already found thyreoglobulin free of iodine obtained from goitrous calves to be without any effect upon the circulation. Oswald further states that thyreoglobulin from hog thyroid containing 0.5 per cent iodine seemed more active than that of the human thyroid with 0.3 per cent iodine.^d

^a cf. F. Blum, *Verhandl. d. Kong. f. inn. Med.*, 1906, **23**, p. 196.

^b A. Oswald, *Arch. f. path. Anat. [etc.]*, Berl., 1902, **169**, p. 461; *Beitr. z. chem. Physiol. u. Path.*, Brnschw., 1902, **2**, p. 555.

^c E. von Cyon and A. Oswald, *Archiv. f. d. ges. Physiol.*, Bonn, 1901, **83**, p. 202.

^d A. Oswald, *Beitr. z. chem. Physiol. u. Path.*, Brnschw., 1902, **2**, p. 556 (footnote).

Marine and Williams^a have recently reported two experiments on the effects of feeding desiccated sheep thyroid containing different percentages of iodine to dogs. Of one preparation which contained 0.0292 per cent iodine 11 grams fed to a dog in eighteen days did not cause a loss of weight, and the fresh thyroid of the dog on analysis yielded but 0.173 milligram iodine per gram. The second preparation had 0.1092 per cent iodine. The dog which received 11 grams of this in eighteen days lost 454 grams weight and its fresh thyroid contained, per gram, 0.439 milligram iodine.

These experiments, although very few in number and not of a character to admit of quantitative results, indicate clearly that there is a relation between the iodine content and the physiological activity of thyroid preparations.

B. EXPERIMENTAL.

METHODS.

None of the methods discussed in the above review are suitable for a quantitative study of the physiological effects of different thyroid preparations. They are all time-consuming, and so do not admit of many experiments; furthermore, they are not adapted for showing small differences in activity. They did not suffice, for example, to demonstrate the physiological activity of thyroid free of iodine. It may also be mentioned that different animals and different patients may react differently to the same preparation;^b this has been observed both clinically and experimentally. If it were possible to test the various thyroid preparations upon the same individual fairly concordant results could probably be obtained, but such experiments are, as a rule, not feasible.

Before beginning the description of the method which forms the basis of the experiments described in this bulletin a few words may be said in regard to some observations which we have made upon the relation between the activity of thyroid preparations and the loss in body weight which their ingestion may produce. Many of the results are given in the protocols of the experiments which follow, but in addition to these several experiments were performed expressly for determining whether a method based upon the loss in weight of the animals could be used for estimating the relative activity of

^a D. Marine and W. W. Williams, *Archives of Internal Medicine*, 1908, **1**, p. 378.

^b The fact that there are such variations in the susceptibility of different individuals can not be considered an argument against the desirability of having thyroid preparations of known strength. It is especially important that when the susceptibility of a patient to a given drug has been determined that treatment should be continued with a preparation of known strength—not with one half or three times as strong, as may readily occur with present commercial thyroid preparations.

thyroid preparations. The figures given in the protocols show the loss of weight for relatively short periods (ten to twenty days) and do not indicate that the method is of practical application. In the special experiments which were undertaken the animals (rats and guinea pigs) were fed during longer periods or until death occurred. The results showed that in general the thyroid with the largest percentage of iodine produced death earliest, but in no case was more than a rough quantitative application of the data possible. It is probable that the primary effect of thyroid feeding is the same in different animals, but that other factors, such as appetite, rate of excretion, etc., which can not be controlled, are involved, and these determine the final result.

The method which we have developed for comparing the physiological activity of different thyroid preparations has for its basis the effect of thyroid feeding upon the resistance of animals to certain poisons. Having found that the administration of thyroid alters the resistance of animals to certain poisons, we performed a large number of experiments in order to determine which poisons were most suitable for comparative studies. The principal poisons tested on mice are included in the following list, and in most cases, as will be seen, negative results were obtained. With many of the compounds in the list but two or three experiments were performed; hence we can not state positively that the feeding of thyroid in these cases had *no* effect upon the resistance to the substance in question. The thyroid, in amounts varying from 0.001 to 0.1 gram per day, was fed in the form of cakes; the poisons were injected subcutaneously:

Acetonecyanhydrine.....	Resistance slightly increased (?)
Acetonitrile.....	Resistance much increased.
Acetylmorphine ("Heroin").....	Resistance diminished.
Antipyrine.....	No effect.
Atropine.....	No effect.
Benzonitrile.....	No effect.
Butylcarbylamine (tertiary).....	No effect.
Caffeine.....	No effect.
Capronitrile.....	No effect.
Chloral hydrate.....	Resistance diminished(?).
Codeine.....	Resistance diminished.
Ethylcarbylamine.....	No effect.
Ethylenecyanide.....	Resistance increased.
Guanidine carbonate.....	No effect.
Guanidine sulphocyanate.....	No effect.
Hydrocyanic acid.....	No effect.
Isovaleraldehydecyanhydrine.....	No effect.
Methylamine.....	No effect.
Methylethylketonecyanhydrine.....	No effect.
Morphine.....	Resistance diminished.
Nicotine.....	No effect.

Nitroprussiate of soda	No effect.
Ox gall	No effect.
Phenol	No effect.
Picrotoxin	No effect.
Sodium arsenate	No effect.
Sodium oxalate	No effect.
Strychnine	No effect.
Trimethylenecyanide	Resistance increased.

The poisons to which the resistance of mice was most markedly altered by the feeding of thyroid were acetonitrile and morphine. Since the susceptibility of rats and guinea pigs to these poisons was also changed by the administration of thyroid, they were selected for comparative studies.

The advantages of a method of this kind are that the experiments are quickly and easily carried out and that they admit of the detection of smaller differences in activity than do the methods hitherto employed. It is not possible to state positively that the physiological activity determined in this manner is in all respects a true index of the therapeutic efficiency of the thyroid, but there are many reasons for believing this to be the case. In the first place, thyroid is pre-eminently a drug that influences metabolism, and the changes in the resistance of animals to the poisons here considered depend upon deep-seated, although little understood, changes in metabolism. In the second place, the results obtained are in complete accord with those observed in clinical studies and with those obtained by other physiological methods. In any case there seems to be much reason for supposing that these reactions are as true an index of the real physiological activity of thyroid as is its effect upon the excretion of urea or upon the circulation.

The experiments were performed upon mice, rats, and guinea pigs. The thyroid was fed to guinea pigs in the form of tablets; to mice and rats in the form of cakes, according to Ehrlich's method. Each cake weighed about 4 grams; mice ate about one cake, rats from one and a half to three cakes per day. The poisons were dissolved in water and injected subcutaneously.

I. EXPERIMENTS WITH ACETONITRILE.

Acetonitrile or methylcyanide, CH_3CN , seems to produce toxic effects chiefly, if not entirely, through the slow liberation in the body of hydrocyanic acid. The views as to the manner in which this formation of hydrocyanic acid takes place have been discussed in a previous bulletin from this laboratory.^a An additional argument for the view that the toxic effects of acetonitrile are due to the formation

^a Bulletin 33: Studies in Experimental Alcoholism, 1907, p. 9.

of hydrocyanic acid may perhaps be found in the comparison of the effects of these two poisons upon sulphur metabolism. In the publication referred to above it was stated that under the influence of acetonitrile the "percentage of sulphur excreted as neutral sulphur frequently rose from 25 to 65 or more; the total excretion was not much changed, but the oxidized sulphur frequently almost disappeared." Results very similar to the above have recently been obtained by Richards and Wallace,^a and by Loewy, Wolf, and Oesterberg^b with potassium cyanide and hydrocyanic acid.

Richards and Wallace found in one experiment upon a dog poisoned with potassium cyanide that while the total amount of sulphur eliminated remained unchanged the percentage eliminated in the oxidized state was 64.53 on the normal day and 48.78 on the day of poisoning. Loewy, Wolf, and Oesterberg found that in severe poisoning by hydrocyanic acid the sulphur eliminated as neutral sulphur increased from 28.6 per cent to 54.8 per cent. The greater effect upon the sulphur metabolism observed in our experiments was probably due to a more prolonged action of the hydrocyanic acid.

As has been already stated, the administration of thyroid causes marked changes in the susceptibility of animals to acetonitrile. Since thyroid does not alter the resistance of animals (or at least of mice) to hydrocyanic acid,^c it may be concluded that its action is exerted chiefly upon the processes by which acetonitrile is decomposed in the body and not upon the hydrocyanic acid which is formed from it. In fact, acetonitrile seems to be a very delicate test for detecting changes in metabolism brought about not only by the thyroid and certain other organ products,^d but by different diets,^e inanition, etc.

^a EXPERIMENTS ON MICE.

Preliminary experiments and theoretical considerations.—When small amounts of thyroid are fed to mice for a few days these animals acquire a markedly increased resistance to acetonitrile. This is true not only for white but also for wild gray mice, although most of the experiments were performed upon the former, and unless otherwise stated, white mice are referred to in all of the following experiments.

The following results may be quoted to illustrate from what large amounts of acetonitrile mice which have received small amounts of

^a A. N. Richards and G. B. Wallace, *J. Biol. Chem.*, 1908, **4**, p. 179.

^b A. Loewy, C. G. L. Wolf, and E. Oesterberg, *Biochem. Ztschr.*, 1908, **8**, p. 132.

^c R. Hunt, *J. Biol. Chem.*, 1906, **1**, p. 42.

^d *J. Am. M. Ass.*, 1907, **49**, p. 1325.

^e *Proc. Soc. Exper. Biol. and Med.*, 1906, **3**, p. 15. These results will soon be published in detail.

thyroid may recover. Only those experiments are quoted which show the maximum non-fatal and the minimum fatal dose:

SERIES I.

A. SHEEP THYROID; 0.179 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
February 1.....	22.62	Feeding of cakes each containing 0.002 gm. thyroid begun.
4.....	23.02	
7.....	22.69	
9.....	23.35	Acetonitrile, 105.08 mgms., i. e., 4.5 mgms. per gm. mouse. Survived.
February 1.....	22.56	Thyroid as above.
4.....	22.18	
7.....	20.62	
10.....	20.28	Acetonitrile, 93.29 mgm., i. e., 4.6 mgms. per gm. mouse. Died 2 hours.

B. CONTROLS.

1908.		
February 1....	18.83	Feeding of cakes without thyroid begun.
4....	20.01	
7....	20.19	
10....	19.02	Acetonitrile, 4.76 mgms., i. e., 0.25 mgm. per gm. mouse. Survived.
February 1....	16.49	Cakes as above.
4....	15.56	
7....	15.79	
10....	16.31	Acetonitrile, 4.24 mgms., i. e., 0.26 mgm. per gm. mouse. Died 10 hours.

Summary.—The results of these experiments may be summarized as follows:

	Gm. thyroid fed daily.	Mgm. I in thyroid.	Weight of mouse in gms.	Amount of acetonitrile in mgms.		Result.
				Per mouse.	Per gm. mouse.	
A.....	0.002	0.0036	23.35	105.08	4.5	Survived.
	.002	.0036	20.28	93.29	4.6	Died.
B.....	0	0	19.02	4.76	.25	Survived.
	0	0	16.31	4.24	.26	Died.

Thus a mouse (A) which had received thyroid recovered from seventeen times the relative amount of acetonitrile fatal to the control. Since 0.25 mgm. per gram is the maximum amount of the nitrile from which a control (B) recovered, we are justified in assuming that this represents the maximum amount of nitrile which the mice of this series could, under normal conditions, neutralize; for a mouse weighing 23.35 gms. this would be a total of 5.84 mgms. The mouse which weighed 23.35 gms. and which had received thyroid recovered, however, from 105.08 mgms. Hence we may conclude that the thyroid had enabled the mouse to neutralize, or resist in some way, 99.24 mgms. acetonitrile. The mice seldom ate an entire cake (containing 0.002 gm. thyroid) in a day; hence they had received less than 20 mgms. thyroid in all.

SERIES II.

A. DOG THYROID; 0.111 PER CENT IODINE

Date.	Weight of mouse.	Remarks.
1908.		
May 9.....	15.83	Feeding of cakes each containing 0.0015 gm. thyroid begun.
16.....	14.05	
18.....	13.94	Acetonitrile, 64.14 mgms., i. e., 4.6 mgms. per gm. mouse. Survived.

B. CONTROLS.

1908.		
May 9.....	19.00	Feeding of cakes without thyroid begun.
16.....	19.86	
18.....	19.52	Acetonitrile, 5.47 mgms., i. e., 0.28 mgm. per gm. mouse. Died 6 hours.

Summary.—The results of these experiments may be summarized as follows:

	Gm. thyroid fed daily.	Mgm. I in thyroid.	Weight of mouse in gms.	Amount of acetonitrile in mgms.		Result.
				Per mouse.	Per gm. mouse.	
A.....	0.0015	0.0017	13.94	64.14	4.6	Survived.
B.....	0	0	19.52	5.47	.28	Died.

The mouse which had received the thyroid recovered from more than sixteen times the relative dose fatal to the controls. A total of less than 15 mgms. of thyroid had led to the physiological neutralization of at least 60.24 mgms. acetonitrile.

SERIES III.

A. SHEEP THYROID; 0.19 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
March 28.....	15.93	Feeding of cakes each containing 0.001 gm. thyroid begun.
31.....	14.88	
April 3.....	15.20	
7.....	14.33	
8.....	14.74	Acetonitrile, 67.80 mgms., i. e., 4.6 mgms. per gm. mouse. Survived.
March 28.....	16.85	Thyroid as above.
31.....	14.24	
April 3.....	14.90	
7.....	14.40	Acetonitrile, 71.12 mgms., i. e., 4.8 mgms. per gm. mouse. Died 1½ hours.

B. CONTROLS.

1908.		
March 28.....	14.30	Feeding of cakes without thyroid begun.
31.....	12.88	
April 3.....	13.15	Acetonitrile, 5.06 mgms., i. e., 0.4 mgm. per gm. mouse. Survived.
7.....	12.64	
March 28.....	15.35	Cakes as above.
31.....	15.06	
April 3.....	13.17	
7.....	12.60	
8.....	12.04	Acetonitrile, 5.06 mgms., i. e., 0.42 mgm. per gm. mouse. Died 1½ hours.

Summary.—The results of these experiments may be tabulated as follows:

	Gm. thyroid fed daily.	Mgm. I in thyroid.	Weight of mouse in gms.	Amount of acetonitrile in mgms.		Result.
				Per mouse.	Per gm. mouse.	
A.....	0.001	0.0019	14.74	67.8	4.6	Survived.
B.....	.001	.0019	14.40	71.12	4.8	Died.
	0	0	12.64	5.06	.4	Survived.
	0	0	12.04	5.06	.42	Died.

The mouse which had received the thyroid recovered from about eleven times the dose fatal to the controls. A total of less than 10 mgms. of thyroid had enabled the mouse to neutralize about 61.8 mgms. acetonitrile.

SERIES IV.

A. SHEEP THYROID; 0.32 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
April 28.....	18.10	Feeding of cakes, each containing 0.0005 gm. thyroid, begun.
May 2.....	19.22	
7.....	18.91	
8.....	18.91	Acetonitrile, 62.40 mgms., i. e., 3.3 mgms. per gm. mouse. Survived.
April 28.....	13.48	Thyroid as above.
May 2.....	14.58	
7.....	15.03	Acetonitrile, 52.60 mgms., i. e., 3.5 mgms. per gm. mouse. Died 6½ hours.

B. CONTROLS.

1908.		
April 28.....	18.98	Feeding of cakes without thyroid begun.
May 2.....	20.34	
7.....	19.53	
8.....		Acetonitrile, 10.94 mgms., i. e., 0.56 mgm. per gm. mouse. Survived.
April 28.....	19.04	Cakes as above.
May 2.....	20.63	
7.....	18.83	
8.....		Acetonitrile, 10.92 mgms., i. e., 0.58 mgm. per gm. mouse. Died 7 hours.

Summary.—The results of these experiments may be tabulated as follows:

	Gm. thyroid fed daily.	Mgm. I in thyroid.	Weight of mouse in gms.	Amount of acetonitrile in mgms.		Result.
				Per mouse.	Per gm. mouse.	
A.....	0.0005	0.0016	18.91	62.4	3.3	Survived.
B.....	.0005	.0016	15.03	52.6	3.5	Died.
	0	0	19.53	10.94	.56	Survived.
	0	0	18.83	10.92	.58	Died.

The mouse which had received the thyroid recovered from a dose of acetonitrile about six times as large as that fatal to the controls. Less than 5 mgms. of thyroid had led to the physiological neutralization of about 51.8 mgms. of acetonitrile.

SERIES V.

A. HOG THYROID; 0.33 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
January 9.....	19.73	Feeding of cakes, each containing 0.0001 gm. thyroid, begun.
14.....	19.50	
17.....	18.82	
19.....	18.80	Acetonitrile, 18.8 mgms., i. e., 1 mgm. per gm. mouse. Survived.
January 9.....	13.83	Thyroid as above.
14.....	15.45	
17.....	14.47	
19.....	13.65	
20.....	13.65	Acetonitrile, 17.75 mgms., i. e., 1.3 mgms. per gm. mouse. Died 2½ hours.

B. CONTROLS.

1907.		
January 9.....	16.45	Feeding of cakes without thyroid begun.
14.....	15.52	
17.....	15.16	
19.....	15.07	Acetonitrile, 5.73 mgms., i. e., 0.38 mgm. per gm. mouse. Survived.
January 9.....	15.25	Cakes as above.
14.....	15.90	
17.....	14.70	
19.....	13.82	
20.....	13.43	Acetonitrile, 5.51 mgms., i. e., 0.41 mgm. per gm. mouse. Died 5 hours.

Summary.—The results of these experiments may be summarized as follows:

	Gm. thyroid fed daily.	Mgm. I in thyroid.	Weight of mouse in gms.	Amount of acetonitrile in mgms.		Result.
				Per mouse.	Per gm. mouse.	
A.....	0.0001	0.00033	18.80	18.8	1.0	Survived.
	.0001	.00033	13.65	17.75	1.3	Died.
B.....	0	0	15.07	5.73	.38	Survived.
	0	0	13.43	5.51	.41	Died.

The mouse which had received thyroid recovered from approximately two and one-half times the dose of acetonitrile fatal to the controls. A total of about 1 mgm. thyroid had enabled the mouse to resist 11.5 mgms. acetonitrile.

We have performed no experiments for the special purpose of determining either the maximum amount of nitrile which may be neutralized under the influence of thyroid or the minimum amount

of thyroid which produces a physiological effect. It is evident, however, from the above that as little as 0.1 mgm. of dry thyroid fed daily for eleven days produced a marked effect; still smaller amounts would doubtlessly have produced a distinct effect.

As was shown in a previous paper,^a this reaction of mice is a very delicate test for thyroid. A few milligrams of thyroid mixed with a large amount of blood or of toasted bread, tamarinds, liquorice powder, etc. (as in the case of a number of the secret "antifat" nostrums), may readily be detected. We have found no other substance with an effect upon the resistance of mice to acetonitrile at all comparable to that of thyroid. This physiological test for thyroid is far more delicate than any chemical method for its detection.^b

In most of our experiments the thyroid was fed for nine or ten days before the injection of the nitrile. This period was selected in part arbitrarily and in part because we were convinced that it was sufficiently long for the maximum effect of the thyroid to have been produced. A very distinct effect was, however, present in a much shorter time; thus mice which had received rather large amounts of an active thyroid preparation for but two days recovered after the injection of twice the dose of nitrile fatal to the controls.

We have few data as to how long the effect of the thyroid continues after the feeding is discontinued. We have observed in some cases, however, that the increased resistance persisted, although it was less, for at least two weeks.

Conditions influencing the resistance of mice to acetonitrile.—Different groups of mice vary in their susceptibility to acetonitrile; hence in carrying out a series of experiments with this substance it is absolutely indispensable to have mice which have been kept under uniform conditions. In testing the effect of thyroid it is also necessary to have a number of controls for each series of experiments. With these precautions we have rarely failed to obtain entirely concordant results and have as a rule determined the fatal dose of the nitrile

^a R. Hunt, J. Am. M. Ass., 1907, 49, p. 240.

^b As was pointed out in the paper referred to above, this method seemed adapted to throw some light on the question whether there is an excessive amount of thyroid secretion in the blood in cases of Grave's disease. So far we have been able to test the blood in only three such cases. In one of these the blood had a marked effect in increasing the resistance of mice to acetonitrile, indicating an excessive amount of thyroid secretion. In another case the results were doubtful; the amount of blood was insufficient for even two experiments. In the third case the results were negative. Possibly this test may have some diagnostic value, although on the thyroid theory of Grave's disease it is not necessary to assume that an excess of thyroid secretion is present in the blood at all times. So far as our observations go it is probable that the best results would be obtained by administering 1 or 2 c. c. of the blood to mice daily for nine or ten days before testing with the nitrile. Several controls (mice fed with normal blood) are indispensable.

to within 0.01 mgm. per gram body weight. The protocols of the experiments described later show what satisfactory results may, with careful work, be obtained.

It has not been possible to determine all the causes of the differences in susceptibility of different groups of mice to acetonitrile. Diet seems, however, to be the most important single factor; mice kept on certain diets for long periods may be many times as resistant as others of the same age and weight kept on a different diet.

Another very important factor in the toxicity is the season. We have records of experiments performed in each month for three and in some cases for four years. Although the diet was approximately the same throughout the year, the mice were invariably more susceptible to the acetonitrile during the summer than during the winter months. The following table shows the average fatal dose (in milligrams per gram) determined during different months:

January.....	0.56	May.....	0.30	September.....	0.25
February.....	.35	June.....	.28	October.....	.39
March.....	.58	July.....	.31	November.....	.45
April.....	.53	August.....	.18	December.....	.55

There were greater variations (in different series of experiments) in the winter than in the summer months, but in only three cases were the figures as low as the average for the summer months. During the winter months the mice were kept in a room heated to 75° F. (23.9° C.); hence it is not probable that the temperature was the only factor.^a

On the manner in which thyroid influences the resistance of mice to acetonitrile.—We are unable to suggest any entirely satisfactory explanation of how the feeding of thyroid protects mice against

^a D. W. Harrington (Am. J. Physiol., 1898, **1**, p. 385) has recorded some very interesting experiments on the relation of season to the susceptibility of the guinea pig to anesthetics and operative procedures; the resistance was very low from February to May and highest from October to January. Stimulation of the vagus was more effective in stopping the heart during the fall and winter than during the spring months. Prof. C. W. Edmunds, of the University of Michigan, found frogs to be much less resistant to digitalis in April than during the summer months.

The following statement of F. C. Koch (Proc. Am. Pharm. Ass., 1907, **55**, p. 371) is very interesting in this connection: "I have recently had occasion to determine the per cent of iodine in unadulterated desiccated sheep thyroids prepared at different seasons during the last two and one-half years, and found that the desiccations without exception test as much as three times higher during the winter months than during June and July, and that the per cent gradually diminished toward the summer months and then again gradually increased toward the winter."

Although it is very probable that the differences found by Koch depend upon differences in diet, it is remarkable that the time of the minimum amount of iodine in sheep thyroid should coincide with the period of least resistance of mice to acetonitrile; as we shall see later the resistance of animals to acetonitrile is closely dependent upon the amount of iodine which their thyroids contain.

acetonitrile. The effect is the reverse of the one which was anticipated from certain theoretical considerations and which led us to perform the experiments. Inasmuch as the view that one of the functions of the thyroid is to neutralize poisons is very widely held and, since the "neutralization" (or rendering harmless) of acetonitrile in the mouse under the influence of thyroid is the only instance^a in which a poison is apparently neutralized in any animal—all the other "poisons" to which reference is so frequently made are purely hypothetical—a few words may be devoted to this subject. In the first place, there is certainly no reason to suppose that there is any direct chemical neutralization of the acetonitrile by the thyroid—an interpretation which some have placed upon our previously published results. Not only is it impossible to think of any way in which such a neutralization could occur, but the amounts of the nitrile which may be rendered harmless are so out of proportion to the amounts of thyroid fed that any such interaction is highly improbable. It was shown in the experiments quoted above that from 1 to 20 mgm. of thyroid fed during the course of nine or ten days enabled mice to resist the toxic effects of from five to ten times an equal weight of acetonitrile. By far the greater part of the thyroid is doubtlessly made up of physiologically inert material; hence the disproportion between the amount of poison "neutralized" and the "neutralizing" agent is still greater. It is interesting to compare in this respect the effect of a very active substance—iodothyrene—derived from the thyroid.

Experiment, February 10, 1908: The iodothyrene used in this experiment was a commercial preparation (Baeyer) stated to contain 1 part of iodothyrene mixed with 309 parts of milk sugar;^b it contained 0.014 per cent iodine.

A. IODOTHYRENE (BAEYER).

Date.	Weight of mouse.	Remarks.
1908.		
February 1....	19.43	Feeding of cakes each containing 0.005 gm. iodothyrene begun.
4....	18.60	
8....	17.55	
9....	17.30	
		Acetonitrile, 43.25 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
February 1....	20.40	Iodothyrene as above.
4....	19.76	
8....	19.70	
10....	19.07	
		Acetonitrile, 49.58 mgms., i. e., 2.6 mgms. per gm. mouse. Died 1 hour.

^a With the exception of two nitriles closely related to acetonitrile (see p. 20-1).

^b See New and Non-Official Remedies, 3d ed., 1908, p. 74.

B. CONTROLS.

Date.	Weight of mouse.	Remarks.
1908.		
February 1....	18.83	Feeding of cakes without iodothyrene.
4....	20.01	
7....	20.19	
10....	19.02	Acetonitrile, 4.76 mgms., i. e., 0.25 mgm. per gm. mouse. Survived.
February 1....	16.49	Cakes as above.
4....	15.56	
7....	15.79	
10....	16.31	Acetonitrile, 4.24 mgms., i. e., 0.26 mgm. per gm. mouse. Died 10 hours.

Summary.—0.005 gm. of the milk sugar trituration was fed; this mixture contained only 1 part of the true iodothyrene in 310. Hence there was fed daily but 0.0161 mgm. iodothyrene. The results are summarized in the following table:

	Mgm. true iodothyrene fed daily.	Mgm. I in true iodothyrene.	Weight of mouse in gms.	Amount of acetonitrile in mgms.		Result.
				Per mouse.	Per gm. mouse.	
A.....	0.0161	0.00000225	17.30	43.25	2.5	Recovered.
	.0161	.00000225	19.07	49.58	2.6	Died.
B.....	0	0	19.02	4.76	.25	Recovered.
	0	0	16.31	4.24	.26	Died.

Thus a mouse (A) which had received iodothyrene recovered from nearly ten times the relative amount of acetonitrile fatal to the controls. Since 0.25 mgm. per gram is the maximum amount of acetonitrile from which a control (B) recovered, we are justified in assuming that this represents the maximum amount of the poison which a mouse of this series could, under normal conditions, neutralize; for a mouse weighing 17.30 gms. (A) this would be a total of 4.33 mgms. The mouse which weighed 17.30 gms. and which had received iodothyrene recovered, however, from 43.25 mgms. Hence we may conclude that the iodothyrene had enabled the mouse to resist in some way the poisonous effects of 38.92 mgms. acetonitrile. The total amount of iodothyrene which the mouse had received in ten days was somewhat less than 0.0161 mgm. Thus one part of true iodothyrene fed to a mouse in the course of ten days had enabled it to resist more than 240 times an equal weight of acetonitrile.

Although we speak of the poison being "neutralized" when a mouse, as a result of the administration of thyroid, recovers from several times the fatal dose of acetonitrile, it is very probable that there has been no neutralization whatever. The effect is probably a preventive one—that is, the thyroid in some way prevents the formation of a poison from the nitrile. The basis of this suggestion is the fact that the feeding of thyroid has no effect upon the toxicity of

hydrocyanic acid itself, the poison produced from the nitrile.^a The thyroid seems to alter the metabolism in such a way that the acetonitrile is disposed of without its breaking down into poisonous constituents, as occurs in the normal animal.^b Were there a direct interaction between the poison and the thyroid the same results would be expected in all classes of animals; but as we shall see, thyroid not only does not protect rats and guinea pigs against acetonitrile, but it increases their susceptibility to this poison.

The activity of the thyroid in relation to acetonitrile is in sharp contrast to that of certain sulphur compounds. The latter are true antidotes for acetonitrile as well as for many other cyanogen compounds.^c The hydrocyanic acid which is formed from these compounds as well as hydrocyanic acid administered as such is neutralized by sulphur with the formation of sulphocyanate; the latter compound is less toxic to warm-blooded animals than the cyanogen compounds themselves. The action of the sulphur compounds is the same in all classes of animals investigated.

An hypothesis similar to that which was advanced above to explain the manner in which the feeding of thyroid increases the resistance of mice to acetonitrile—that the thyroid simply alters metabolic processes in such a way that a poisonous substance is not produced from the nitrile—seems sufficient to explain what is frequently called the detoxicatory action of the thyroid. In the normal organism the thyroid probably has a directing influence upon metabolism of such a character that all the products of metabolism are converted into useful or at least harmless compounds. In the absence of the thyroid the metabolism probably proceeds along abnormal lines, with the result that substances necessary for the proper functioning of certain organs are not formed; possibly poisonous substances are also produced, although the evidence is against this supposition.^d This hypothesis seems more reasonable than one assuming that poisonous substances are normally produced and that an organ has been evolved for the purpose of neutralizing them.

^a This argument is, of course, by no means conclusive. It is possible that after the feeding of thyroid hydrocyanic acid is produced from the nitrile, but in such a manner or in a place where it can be neutralized by the body, whereas when hydrocyanic acid itself is administered it may not reach the cells or parts of cells where neutralization is possible. A study of the sulphocyanate excretion of thyroid fed mice after the administration of acetonitrile might throw some light on this subject.

^b Another possibility which may be considered in this connection is that mice may, under the influence of thyroid, utilize acetonitrile for the synthesis of protein or other nitrogen-containing bodies. Latham (*Biochem. J.*, 1908, **3**, p. 193) believes that certain nitriles are utilized in this way in the normal animal.

^c See R. Hunt, *Arch. internat. de pharmacodyn. e. d. ther.*, 1904, **12**, p. 447.

^d The blood of thyroidectomized animals is not, according to a number of writers, toxic; cf. L. Launoy, *Semaine méd. Par.*, 1908, **28**, p. 382; D. Baldi, *Arch. ital. de biol.*, Turin, 1899, **31**, p. 281.

It seems unnecessary to divide the functions of the thyroid into "metabolic" and "detoxicatory," as is sometimes done. It is sufficient to recognize that the thyroid has certain effects—for the most part unknown—upon metabolism. Under normal conditions these effects lead to the formation of useful substances or promote in other ways cellular activities. When an unusual poison, such as acetonitrile, is introduced into an animal under the influence of thyroid, its fate will depend upon how the animal's metabolism as regards this poison has been affected by the thyroid; the latter alters the metabolism of the mouse in such a way that the acetonitrile is rendered harmless or is prevented from becoming harmful, but it alters the metabolic processes of rats and guinea pigs in such a way that the acetonitrile becomes much more harmful. In a somewhat similar way certain processes of oxidation proceed along definite lines; for instance, when a poison such as ethyl alcohol is introduced into the body these processes of oxidation destroy it, thus not only making it harmless, but the body is enabled to utilize the energy set free. In the case of methyl alcohol, however, although the oxidation may proceed along similar lines, part of the alcohol is converted into substances (formaldehyde and formic acid) more poisonous than the original substance. The fate of acetonitrile in the body of a mouse to which thyroid has been administered may be compared to the fate of ethyl alcohol; that of acetonitrile in the body of a rat which has received thyroid to that of methyl alcohol.

i. EXPERIMENTS WITH "IODINE FREE" THYROID.^a

The question whether thyroid free of iodine has any physiological activity has, like the entire question of the relation of iodine to the thyroid, been approached from two points of view. Those who have considered it from the standpoint of the activity of a living gland in

^a By "iodine free" thyroid we mean thyroid which does not give even a qualitative test for iodine when 1 gm. of sample is examined by the Baumann method. The limit of this method when applied to a complex body like the thyroid, which contains a very large amount of organic matter, is about 0.01 per cent; although somewhat smaller amounts of iodine could be satisfactorily estimated by using more than 1 gm. of material. As is well known, Paul Bourcet (*Compt. rend. Acad. d. sc.*, Par. 1899, **128**, p. 1120) modified the Baumann method so that very much smaller amounts of iodine could be determined when 50 to 1,000 gms. of the material were employed. The modification consists in concentrating the solution of the fused mass obtained by the incineration of the sample and removing the potassium sulphate by repeated precipitation with alcohol. By this method Bourcet was able to estimate as small an amount as 0.1 mgm. of iodine per kilogram of sample. A. R. Dochez (*Johns Hopkins Hospital Bull.* 1908, **19**, p. 235) using this method, found iodine in crystallized cane sugar, egg yolk, "C. P. glucose," and in a very large number of other ordinary foods. Of the substances examined only C. P. lactose, egg albumen, chocolate, almonds, and pig embryos (thyroids excised) were reported as containing no iodine.

It is very probable that the thyroid which we call "iodine free" would have been found to contain iodine if examined by Bourcet's modification, and it is also possible

the body have assumed that such thyroid is active (Neumeister, Miwa and Stoeltzner, Hutchinson). Those, on the other hand, who have studied the question from the pharmacological side, i. e., in the same way as other drugs are studied, have denied that such thyroid has any physiological activity (Roos, Oswald, Von Cyon and Oswald).

One of the present writers^a stated in a preliminary paper that he had found thyroid free of iodine to have a low degree of physiological activity. The experiments upon which this statement was based will now be described in detail.

The thyroid most frequently used in these experiments was obtained from infants who had died of various diseases. About 80 such glands were dried at 50° to 60° C., powdered, and thoroughly mixed. There were also available small amounts of thyroid from Maltese kids, an Alaskan bear, and an aoudad.^b None of these preparations, when examined by the usual method for detecting iodine in the thyroid, gave even a qualitative test for this element.^c

That the thyroids of children usually contain little or no iodine was first pointed out by Baumann.^d This investigator found that the presence or absence of iodine and the amount of the latter, when present, varied according to the locality from which the glands were obtained. Nine of twelve thyroids of infants under 1½ years of age, from Freiburg, contained no iodine; three contained from 0.007 to 0.015 per cent. Of six infants from Berlin 1½ years or less of age the thyroids of five contained from 0.014 to 0.033 per cent of iodine; those of the sixth contained none. The thyroids of six children from Hamburg had an average iodine content of 0.07 per cent.

Miwa and Stöltzner^e examined the thyroids of twelve infants from Berlin; in but one was iodine found, and then only to the extent of 0.025 per cent. Weiss^f examined the thyroids of seven children under 4¼ years; the iodine varied from traces to 0.037 per cent.

that these traces of iodine are responsible for the physiological effects we attribute to "iodine free" thyroid. On the other hand, if these thyroids were found to contain traces of iodine it does not follow that this iodine was in the form of combination peculiar to the thyroid.

^a R. Hunt, J. Am. M. Ass., Chicago, 1907, **49**, 1324.

^b We are much indebted to Dr. J. R. Mohler, Chief of the Division of Pathology, Bureau of Animal Industry, Department of Agriculture, and pathologist to the National Zoological Park, for the thyroids of these and of a number of other rare animals. The children's thyroids were obtained from Baltimore. In this connection it may be mentioned that H. G. Wells (J. Am. M. Ass., 1897, **29**, p. 1011) found the average percentage of iodine in the thyroid of six adults of Baltimore to be 0.236.

^c Two gms. of the children's thyroids, 1 of the Maltese kids, 1 of the Alaskan bear, and 0.3 of the aoudad were used for the tests.

^d E. Baumann, Ztschr. f. physiol. Chem., Strassb., 1896, **22**, p. 11.

^e S. Miwa and W. Stöltzner, Jahrb. f. Kinderh., 1897, **45**, p. 87.

^f F. Weiss, München. med. Wehnschr., 1897, **44**, p. 6.

Wells^a analyzed the thyroids of six children from Chicago under 4 years; three had but traces, the other three from 0.011 to 0.092 per cent. Von Rositzky^b reported analyses of the thyroids of eight children under 10 years of age; the percentage of iodine varied from 0.012 to 0.041. Oswald^c found in five children from Basel under 7 years from traces to 0.061 per cent iodine. Charrin and Bourcet^d found in the thyroid of infants under 3 months who were born of healthy mothers from 0.0004 to 0.0054 per cent iodine. In many cases in which the child or mother had suffered from various diseases no iodine was found. Mendel^e found no iodine in the thyroids of four infants; that of a fifth contained 0.07 mgm. Jolin^f found in twenty-seven infants in Sweden under 4 years no distinct traces of iodine in seven cases and from traces to 0.086 per cent in the others. Nagel and Roos^g found no iodine in the thyroids of four new-born puppies.

The following experiments were performed with the iodine free preparations described above. A few experiments with thyroid containing various amounts of iodine are quoted for comparison. In all cases the dried and powdered gland was used.

SERIES I.

A. THYROID OF CHILDREN; FREE OF IODINE.

Date.	Weight of mouse.	Remarks.
1906.		
February 24....	22.06	Feeding of cakes each containing 0.05 gm. thyroid begun.
March 3.....	22.85	
6.....	22.15	Acetonitrile, 17.72 mgms., i. e., 0.8 mgm. per gm. mouse. Survived.
7.....		Acetonitrile, 26.58 mgms., i. e., 1.2 mgms. per gm. mouse. Survived.
February 24....	17.22	Thyroid as above.
March 3.....	18.05	
6.....	17.75	Acetonitrile, 17.75 mgms., i. e., 1 mgm. per gm. mouse. Survived.
7.....		Acetonitrile, 24.85 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.

B. CONTROLS.

1906.		
February 21....	20.75	Cakes without thyroid.
March 3.....	19.85	
6.....	18.75	Acetonitrile, 5.63 mgm., i. e., 0.3 mgm. per gm. mouse. Died 2 hours.
February 21....	22.71	Cakes without thyroid.
March 3.....	22.55	
6.....	20.95	Acetonitrile, 7.33 mgms., i. e., 0.35 mgm. per gm. mouse. Died 1 to 3 hours.
February 21....	23.71	Cakes without thyroid.
March 3.....	25.35	
6.....	24.45	Acetonitrile, 12.23 mgms., i. e., 0.5 mgm. per gm. mouse. Died 1 hour.

^a H. G. Wells, J. Am. M. Ass., Chicago, 1897, **29**, p. 955.

^b A. v. Rositzky, Wien. klin. Wchnschr., 1897, **37**, p. 823.

^c A. Oswald, Ztschr. f. physiol. Chem., Strassb., 1897, **23**, p. 291.

^d A. Charrin and P. Bourcet, Compt. rend. Acad. d. sc., Par. 1900, **130**, p. 945.

^e L. B. Mendel, Am. J. Physiol., Boston, 1900, **3**, p. 287.

^f S. Jolin, Festschrift O. Hammarsten, Upsala, 1906.

^g W. A. Nagel and E. Roos, Arch. f. (Anat. u.) Physiol., Suppl. Bd., 1902, p. 275.

Summary.—The results of the above experiments may be summarized as follows:

Thyroid.	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Fatal dose of acetonitrile in mgms. per gm.	
			Recovered.	Died.
A. Children's.....	0.05	0	1.4
B. Controls.....				0.3

Unfortunately the experiments were not sufficiently numerous for the fatal doses to be determined, but it is evident that the children's thyroid had protected the mice against at least five times the dose of acetonitrile fatal to the controls.

SERIES II.

A. CHILDREN'S THYROID; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1906.		
July 28.....	20.51	Feeding of cakes each containing 0.05 gm. thyroid begun.
30.....	20.40	
August 3.....	19.00	
7.....	16.80	
9.....	15.69	Acetonitrile, 31.38 mgms., i. e., 2 mgms. per gm. mouse. Survived.
July 28.....	21.63	Thyroid as above.
30.....	20.96	
August 3.....	21.00	
7.....	19.00	
9.....	18.50	
10.....	18.50	Acetonitrile, 38.85 mgms., i. e., 2.1 mgms. per gm. mouse. Died 1½ hours.

B. SHEEP THYROID; 0.176 PER CENT IODINE.

1906.		
July 28.....	23.71	Feeding of cakes each containing 0.05 gm. thyroid begun.
30.....	22.79	
August 3.....	20.39	
7.....	17.91	Acetonitrile, 25.07 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.
July 28.....	24.52	Thyroid as above.
30.....	21.14	
August 3.....	19.00	
7.....	15.70	
8.....	15.25	Acetonitrile, 30.5 mgms., i. e., 2 mgms. per gm. mouse. Survived.
July 28.....	15.81	Thyroid as above.
30.....	16.53	
August 3.....	16.56	
7.....	17.50	
9.....	14.33	Acetonitrile, 32.96 mgms., i. e., 2.3 mgms. per gm. mouse. Died 1½ hours.
July 28.....	14.11	Thyroid as above.
30.....	14.36	
August 3.....	14.08	
4.....	12.78	
9.....	12.41	Acetonitrile, 32.27 mgms., i. e., 2.6 mgms. per gm. mouse. Died 2 hours.

C. CONTROLS.

Date.	Weight of mouse.	Remarks.
1906.		
July 28.....	22.42	Cakes without thyroid
30.....	23.51	
August 3.....	24.70	
7.....	22.83	
8.....	21.91	Acetonitrile, 3.07 mgms., i. e., 0.14 mgm. per gm. mouse. Survived.
July 28.....	27.68	Cakes without thyroid.
30.....	28.02	
August 3.....	28.73	
7.....	27.04	
9.....	24.61	Acetonitrile, 4.18 mgms., i. e., 0.17 mgm. per gm. mouse. Survived.
July 28.....	22.33	Cakes without thyroid.
30.....	21.62	
August 3.....	21.11	
7.....	18.42	
8.....	17.58	Acetonitrile, 3.52 mgms., i. e., 0.20 mgm. per gm. mouse. Died 1 to 2 hours.
July 28.....	21.85	Cakes without thyroid.
30.....	22.30	
August 3.....	22.06	
7.....	20.77	Acetonitrile, 5.19 mgms., i. e., 0.25 mgm. per gm. mouse. Died 1½ hours.

Summary.—The results of the above experiments may be summarized as follows:

Thyroid.	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A. Children's.....	0.05	0	0	2.0	2.1
B. Sheep.....	.05	.176	.088	2.0	2.3
C. Controls.....				.17	.2

In these experiments both the children's and sheep's thyroids protected against ten times the fatal dose of acetonitrile; the iodine free children's thyroids were as effective as the iodine containing sheep's thyroids. But, as appears from the following experiments, too much thyroid had been given to admit of comparison—that is, the maximum effect had been produced in each case.

In the next series smaller amounts of children's thyroid were fed and the results compared with those obtained with guinea pig's thyroid; the latter contained 0.05 per cent iodine.

SERIES III.

A. CHILDREN'S THYROID; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1907.		
April 5.....	23.33	Feeding of cakes each containing 0.02 gm. thyroid begun.
8.....	22.66	
11.....	21.42	
15.....	19.92	Acetonitrile, 9.96 mgms., i. e., 0.5 mgm. per gm. mouse. Survived.
April 5.....	23.35	Thyroids as above.
8.....	23.31	
11.....	23.95	
15.....	24.22	
16.....	23.82	Acetonitrile, 14.29 mgms., i. e., 0.6 mgm. per gm. mouse. Died 2 hours.
April 5.....	26.50	Thyroid as above.
8.....	26.46	
11.....	25.35	
14.....	24.32	Acetonitrile, 17.02 mgms., i. e., 0.7 mgm. per gm. mouse. Died about 9 hours.

B. GUINEA PIG THYROID; 0.05 PER CENT IODINE.

1907.		
April 5.....		Feeding of cakes each containing 0.0035 gm. thyroid commenced.
8.....	14.65	
11.....	16.02	
15.....	15.62	Acetonitrile, 9.37 mgms., i. e., 0.6 mgm. per gm. mouse. Survived.
April 5.....		Thyroid as above.
8.....	18.72	
11.....	18.68	
15.....	17.50	
16.....	17.82	Acetonitrile, 14.26 mgms., i. e., 0.8 mgm. per gm. mouse. Survived.
April 5.....		Thyroid as above.
8.....	17.85	
11.....	18.27	
15.....	18.60	Acetonitrile, 18.60 mgms., i. e., 1 mgm. per gm. mouse. Died 3½ hours.

C. CONTROLS.

1907.		
April 5.....	23.01	Cakes without thyroid.
8.....	21.85	
11.....	22.42	
15.....	22.52	Acetonitrile, 6.76 mgms., i. e., 0.3 mgm. per gm. mouse. Survived.
April 5.....	18.06	Cakes as above.
8.....	15.32	
11.....	15.32	
15.....	14.90	
16.....	15.45	Acetonitrile, 5.41 mgms., i. e., 0.35 mgm. per gm. mouse. Died 2½ hours.
April 5.....	18.01	Cakes as above.
8.....	15.36	
11.....	16.00	
14.....	15.40	Acetonitrile, 6.16 mgms., i. e., 0.4 mgm. per gm. mouse. Died about 11¾ hours.

Summary.—The results of the above experiments may be summarized as follows:

Thyroid.	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed.	Fatal dose acetonitrile in mgm. per gm. mouse.	
				Recovered.	Died.
A. Children	0.02	0	0	0.5	0.6
B. Guinea pig0035	.05	.0017	.8	1.0
C. Controls3	.35

Thus the mice which had received the guinea pig thyroid (B) recovered from about one and five-tenths times the dose of acetonitrile fatal to the mice which had received the children's thyroid (A). Five and seven-tenths times as much of the children's thyroid as of the guinea pig's thyroid had been fed; hence we may conclude that the latter was approximately eight and five-tenths times as active as the former.

SERIES IV.

A. THYROID OF MALTESE KID;^a NO IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
April 27.....	12.33	Feeding of cakes each containing 0.05 gm. thyroid begun
30.....	12.67	
May 3.....	12.65	Acetonitrile, 8.75 mgms., i. e., 0.7 mgm. per gm. mouse. Survived.
4.....	12.50	
April 27.....	20.93	Thyroid as above.
30.....	19.82	
May 3.....	20.82	
4.....	21.67	
7.....	21.73	
10.....	22.71	
14.....	22.95	Acetonitrile, 20.66 mgms., i. e., 0.9 mgm. per gm. mouse. Died 2 hours.
April 27.....	22.53	Thyroid as above.
30.....	19.51	
May 3.....	21.87	
4.....	22.42	
7.....	22.61	
10.....	22.91	
13.....	22.85	Acetonitrile, 27.42 mgms., i. e., 1.2 mgms per gm. mouse. Died 4 hours.

^a Unfortunately no microscopic examination was made of these glands. They weighed 17.65 gms. fresh; 3.25 gms. dry. Thus more than 81.5 per cent consisted of water. They were apparently abnormal (glandular hyperplasia?).

B. CHILDREN'S THYROID; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1907.		
April 27.....	11.90	Feeding of cakes each containing 0.05 gm. thyroid begun.
30.....	12.55	
May 3.....	12.76	
4.....	12.27	Acetonitrile, 8.59 mgms., i. e., 0.7 mgm. per gm. mouse. Survived.
April 27.....	15.01	Thyroid as above.
30.....	15.15	
May 3.....	15.45	
4.....	15.58	Acetonitrile, 14.39 mgms., i. e., 1 mgm. per gm. mouse. Survived.
7.....	15.67	
10.....	15.21	
13.....	14.39	
April 27.....	20.11	
30.....	19.27	Thyroid as above.
May 3.....	18.60	
4.....	18.25	
7.....	18.17	Acetonitrile, 18.99 mgms., i. e., 1.2 mgms. per gm. mouse. Survived.
10.....	17.71	
14.....	15.83	

C. GUINEA PIG THYROID; 0.05 PER CENT IODINE.

1907.		
April 27.....	13.73	Feeding of cakes each containing 0.007 gm. thyroid begun.
30.....	13.00	
May 3.....	12.42	
4.....	12.80	Acetonitrile, 10.24 mgms., i. e., 0.8 mgm. per gm. mouse. Survived.
April 27.....	12.65	Thyroid as above.
30.....	13.42	
May 3.....	13.32	
7.....	12.76	Acetonitrile, 11.47 mgms., i. e., 1 mgm. per gm. mouse. Survived.
10.....	12.01	
13.....	11.47	
April 27.....	17.12	
30.....	17.40	
May 3.....	17.12	Thyroid as above.
4.....	16.25	
7.....	15.61	
10.....	15.83	Acetonitrile, 22.80 mgms., i. e., 1.5 mgms. per gm. mouse. Survived.
13.....	15.20	
April 27.....	24.35	
30.....	24.83	Thyroid as above.
May 3.....	24.32	
4.....	24.06	
7.....	24.56	Acetonitrile, 49.34 mgms., i. e., 2 mgms. per gm. mouse. Survived.
10.....	24.53	
14.....	24.67	

D. CONTROLS.

Date.	Weight of mouse.	Remarks.
1907.		
April 27.....	13.63	Cakes without thyroid.
May 3.....	13.95	
4.....	13.52	Acetonitrile, 3.38 mgms., i. e., 0.25 mgm. per gm. mouse. Survived.
April 27.....	15.62	Cakes as above.
30.....	16.65	
May 3.....	15.43	
7.....	14.91	
10.....	14.35	
14.....	14.02	Acetonitrile, 3.93 mgms., i. e., 0.28 mgm. per gm. mouse. Died 2½ hours.
April 27.....	13.12	Cakes as above.
30.....	13.07	
May 3.....	12.33	
4.....	12.02	
7.....	11.45	
10.....	11.55	
13.....	11.25	Acetonitrile, 3.94 mgms., i. e., 0.35 mgm. per gm. mouse. Died 7 hours.
April 27.....	20.57	Cakes as above.
30.....	21.40	
May 3.....	20.00	
4.....	20.32	Acetonitrile, 10.16 mgms., i. e., 0.5 mgm. per gm. mouse. Died 10 hours.

Summary.—These results may be tabulated as follows:

Thyroid.	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mg. I in thyroid fed.	Fatal dose of acetonitrile in mgms. per gm. mouse.	
				Recovered.	Died.
A. Maltese kid	0.05	0	0	0.7	0.9
B. Children05	0	0	1.2
C. Guinea pig007	.05	.0035	2.0
D. Controls.....25	.28

Unfortunately the experiments were not sufficiently numerous to permit of a determination of the fatal dose in all cases. The guinea pig thyroid (C) protected against more than twice as much acetonitrile as did the thyroid of the Maltese kid (A); since seven times as much of the latter as of the former was given, we may consider that the guinea pig thyroid is more than fourteen times as active as that of the Maltese kid. Another point of interest in this series is that the children's thyroid (B) was more active than the Maltese kid thyroid; this shows that there are differences in activity of different "iodine free" thyroids.

Owing to lack of material but few experiments were made with smaller amounts of children's thyroid and the results were not altogether satisfactory; 1 mgm. fed daily for ten days had slight, if any, effect.

SERIES V.

A. THYROID OF ALASKAN BEAR; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1908.		
May 19.....	16.54	Feeding of cakes each containing 0.005 gm. thyroid begun.
23.....	15.49	
27.....	15.25	Acetonitrile, 6.87 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
May 19.....	11.83	Thyroid as above.
23.....	11.35	
27.....	10.13	
28.....		Acetonitrile, 4.86 mgms., i. e., 0.48 mgm. per gm. mouse. Survived.
May 19.....	16.75	Thyroid as above.
23.....	16.77	
27.....	16.23	Acetonitrile, 8.44 mgms., i. e., 0.52 mgm. per gm. mouse. Died 2½ hours.
May 19.....	17.43	Thyroid as above.
23.....	16.66	
27.....	16.33	Acetonitrile, 9.80 mgms., i. e., 0.60 mgm. per gm. mouse. Died 1½ hours.

B. THYROID OF AOUDAD; IODINE FREE.

1908.		
May 19.....	15.39	Feeding of cakes each containing 0.005 gm. thyroid begun.
23.....	17.03	
27.....	16.00	
28.....		Acetonitrile, 6.40 mgms., i. e., 0.40 mgm. per gm. mouse. Died 1½ hours.
May 19.....	15.87	Thyroid as above.
23.....	15.73	
27.....	14.65	Acetonitrile, 7.62 mgms., i. e., 0.52 mgm. per gm. mouse. Died 2½ hours
May 19.....	15.07	Thyroid as above.
23.....	14.30	
27.....	13.50	Acetonitrile, 8.10 mgms., i. e., 0.60 mgm. per gm. mouse. Died 2 hours.

C. THYROID OF BLACK LEOPARD; 0.01 PER CENT IODINE.

1908.		
May 19.....	19.12	Feeding of cakes, each containing 0.005 gm. thyroid begun.
23.....	18.15	
27.....	18.99	
28.....		Acetonitrile, 9.50 mgms., i. e., 0.50 mgm. per gm. mouse. Died 1¼ hours.
May 19.....	18.03	Thyroid as above.
23.....	17.32	
27.....	16.65	Acetonitrile, 11.66 mgms., i. e., 0.70 mgm. per gm. mouse. Died 2¼ hours.
May 19.....	19.04	Thyroid as above.
23.....	18.78	
27.....	18.56	Acetonitrile, 16.70 mgms., i. e., 0.90 mgm. per gm. mouse. Died 3 hours.

D. THYRADEN; ^a 0.085 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
May 19.....	15.50	Feeding of cakes each containing 0.00125 gm. thyraden begun.
23.....	14.81	
27.....	13.12	Acetonitrile, 9.18 mgms., i. e., 0.7 mgm. per gm. mouse. Survived.
May 19.....	18.46	Thyroid as above.
23.....	17.30	
28.....	16.23	Acetonitrile, 12.98 mgms., i. e., 0.8 mgm. per gm. mouse. Survived.
May 19.....	15.19	Thyroid as above.
23.....	15.03	
27.....	14.65	Acetonitrile, 13.19 mgms., i. e., 0.9 mgm. per gm. mouse. Died 1 hour.
May 19.....	16.69	Thyroid as above.
23.....	14.53	
27.....	14.02	Acetonitrile, 14.02 mgms., i. e., 1 mgm. per gm. mouse. Died 1½ hours.

^aThis is a commercial lactose trituration of dried thyroid claimed to be standardized to contain 0.07 per cent iodine. Two specimens examined by us were found to contain slightly more iodine than this, viz. 0.085 per cent.

E. CONTROLS.

1908.		
May 19.....	15.79	Feeding of cakes without thyroid begun.
23.....	15.65	
27.....	15.87	Acetonitrile, 3.97 mgms., i. e., 0.25 mgm. per gm. mouse. Survived.
May 19.....	15.66	Cakes as above.
23.....	15.24	
27.....	16.02	
28.....		Acetonitrile, 4.17 mgms., i. e., 0.26 mgm. per gm. mouse. Died 4½ hours.
May 19.....	17.55	Cakes as above.
23.....	18.15	
28.....	18.10	Acetonitrile, 5.43 mgms., i. e., 0.30 mgm. per gm. mouse. Died 2 hours.
May 19.....	11.80	Cakes as above.
23.....	11.70	
27.....	10.34	Acetonitrile, 3.31 mgms., i. e., 0.32 mgm. per gm. mouse. Died 3 hours.

Summary.—The results of the above experiments may be summarized as follows:

Thyroid.	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed.	Fatal dose of acetonitrile in mgm. per gm. mouse.	
				Recovered.	Died.
A. Alaskan bear.....	0.005	0	0	0.48	0.52
B. Aoudad.....	.005	0	040
C. Black leopard.....	.005	.01	.000150
D. Thyraden.....	.00125	.085	.0011	.80	.90
E. Controls.....				.25	.26

The iodine free thyroid of the Alaskan bear (A) had some physiological activity, but it was much (perhaps about seven times) less than that of Thyraden (D), with 0.085 per cent iodine. The iodine free thyroid of the aoudad (B) was evidently less active than that of the Alaskan bear; in fact, there is nothing in this series to indicate that it had any activity whatever, but perhaps the doses of acetonitrile were too large. A point of interest is the fact that the thyroid of the black leopard (C), which contained 0.01 per cent iodine, was certainly not more active than the "iodine free" thyroid of the Alaskan bear. Of course it is possible that there was a small amount of iodine in the latter which was overlooked in the analysis; unless this is the case (and the probabilities are that it is not) we must conclude that at times iodine free thyroid is as active as thyroid containing a minimum amount of iodine.

SERIES VI.

A. THYROID OF MALTESE KID; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1908.		
September 5...	17.60	Feeding of cakes each containing 0.01 gm. thyroid commenced.
9...	17.24	
12...	16.90	
14...	16.02	Acetonitrile, 4 mgms., i. e., 0.25 mgm. per gm. mouse. Survived.
September 5...	18.76	Thyroid as above.
9...	18.02	
12...	17.72	
14...	17.13	Acetonitrile, 4.62 mgms., i. e., 0.27 mgm. per gm. mouse. Died 2 hours.
September 5...	18.75	Thyroid as above.
9...	19.70	
12...	19.54	
13...	Acetonitrile, 5.86 mgms., i. e., 0.3 mgm. per gm. mouse. Died 2½ hours.
September 5...	19.40	Thyroid as above.
9...	17.30	
12...	17.04	
13...	Acetonitrile, 7.67 mgms., i. e., 0.45 mgm. per gm. mouse. Died 1½ hours.

B. THYROID OF ALASKAN BEAR; IODINE FREE.

1908.		
September 5...	17.40	Feeding of cakes each containing 0.01 gm. thyroid commenced.
9...	17.82	
12...	18.88	
14...	19.02	Acetonitrile, 8.56 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
September 5...	15.24	Thyroid as above.
9...	14.46	
12...	14.80	
13...	Acetonitrile, 7.4 mgms., i. e., 0.5 mgm. per gm. mouse. Survived.
September 5...	20.24	Thyroid as above.
9...	20.08	
12...	19.28	
14...	18.94	Acetonitrile, 10.04 mgms., i. e., 0.53 mgm. per gm. mouse. Died 1½ hours.
September 5...	19.00	Thyroid as above.
9...	18.76	
12...	18.00	
13...	Acetonitrile, 10.8 mgms., i. e., 0.6 mgm. per gm. mouse. Died 3 hours.

C. THYROID OF CHILDREN; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1908.		
September 5...	19.88	Feeding of cakes each containing 0.01 gm. thyroid commenced.
9...	20.92	
12...	19.94	
13...	Acetonitrile, 8.97 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
September 5...	14.84	Thyroid as above.
9...	16.20	
12...	16.26	
14...	15.95	Acetonitrile, 8.45 mgms., i. e., 0.53 mgm. per gm. mouse. Survived.
September 5...	17.06	Thyroid as above.
9...	15.80	
12...	16.00	
14...	15.13	Acetonitrile, 8.62 mgms., i. e., 0.57 mgm. per gm. mouse. Died 1½ hours.
September 5...	15.68	Thyroid as above.
9...	14.42	
12...	14.24	
13...	Acetonitrile, 8.54 mgms., i. e., 0.6 mgm. per gm. mouse. Died 8 hours.

D. THYROID OF BLACK LEOPARD; 0.01 PER CENT IODINE.

1908.		
September 5...	17.14	Feeding of cakes each containing 0.01 gm. thyroid commenced.
9...	18.10	
12...	17.68	
14...	17.23	Acetonitrile, 4.31 mgms., i. e., 0.25 mgm. per gm. mouse. Survived.
September 5...	18.08	Thyroid as above.
9...	18.22	
12...	18.18	
14...	17.85	Acetonitrile, 4.82 mgms., i. e., 0.27 mgm. per gm. mouse. Survived.
September 5...	19.00	Thyroid as above.
9...	19.52	
12...	19.24	
13...	Acetonitrile, 5.77 mgms., i. e., 0.3 mgm. per gm. mouse. Died 2½ hours.
September 5...	17.08	Thyroid as above.
9...	16.92	
12...	16.78	
13...	Acetonitrile, 7.55 mgms., i. e., 0.45 mgm. per gm. mouse. Died 2 hours.

E. THYROID OF SHEEP; 0.125 PER CENT IODINE.

1908.		
September 5...	18.56	Feeding of cakes each containing 0.001 gm. thyroid commenced.
9...	19.16	
12...	18.54	
13...	Acetonitrile, 27.81 mgms., i. e., 1.5 mgms. per gm. mouse. Survived.
September 5...	19.52	Thyroid as above.
9...	19.98	
12...	18.16	
14...	19.25	Acetonitrile, 30.8 mgms., i. e., 1.6 mgms. per gm. mouse. Survived.
September 5...	21.44	Thyroid as above.
9...	19.00	
12...	18.52	
13...	Acetonitrile, 31.48 mgms., i. e., 1.7 mgms. per gm. mouse. Died 1 hour.
September 5...	18.00	Thyroid as above.
9...	18.43	
12...	18.24	
14...	16.98	Acetonitrile, 30.56 mgms., i. e., 1.8 mgms. per gm. mouse. Died 2¼ hours.

F. CONTROLS.

Date.	Weight of mouse.	Remarks.
1908.		
September 5...	18.04	Feeding of cakes without thyroid commenced.
9...	17.50	
12...	17.20	
14...	17.00	Acetonitrile, 1.87 mgms., i. e., 0.11 mgm. per gm. mouse. Survived.
September 5...	19.78	Cakes as above.
9...	20.50	
12...	20.56	
14...	20.29	Acetonitrile, 2.64 mgms., i. e., 0.13 mgm. per gm. mouse. Died 2½ hours.
September 5...	21.14	Cakes as above.
9...	20.52	
12...	20.48	
14...	20.22	Acetonitrile, 3.03 mgms., i. e., 0.15 mgm. per gm. mouse. Died 3 hours.
September 5...	21.32	Cakes as above.
9...	22.16	
12...	22.40	
13...		Acetonitrile, 4.03 mgms., i. e., 0.18 mgm. per gm. mouse. Died 5 hours.

SUMMARY.

Thyroid.	Gm. thy- roid fed daily.	Percent- age of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of ace- tonitrile in mgms. per gm.	
				Recovered.	Died.
A. Maltese kid.....	0.01	0	0	0.25	0.27
B. Alaskan bear.....	.01	0	0	.50	.53
C. Children.....	.01	0	0	.53	.57
D. Black leopard.....	.01	.01	.001	.27	.30
E. Sheep.....	.001	.125	.00125	1.60	1.70
F. Controls.....				.11	.13

The three iodine free thyroids (A, B, and C) protected mice against more than twice the dose of acetonitrile fatal to the controls; those of the Alaskan bear and of children were about twice as active as that of the Maltese kid. The thyroid of the black leopard, although it contained a small percentage of iodine, was only about half as active as the thyroids of the Alaskan bear and of the children. One one-thousandth of a gram of sheep thyroid, containing 0.125 per cent iodine, protected against about three times as much acetonitrile as did ten times as much of the iodine free children's thyroid; we may therefore conclude that it was about thirty times as active as the latter.

SERIES VII.

A. THYROID OF ALASKAN BEAR; IODINE FREE.

Date.	Weight of mouse.	Remarks.
1908.		
June 1.....	17.06	Feeding of cakes each containing 0.01 gm. thyroid begun.
5.....	15.45	
9.....	15.00	
10.....		Acetonitrile, 3.90 mgms., i. e., 0.26 mgm. per gm. mouse. Survived.
June 1.....	17.50	Thyroid as above.
5.....	15.28	
9.....	15.68	
11.....	16.32	Acetonitrile, 5.06 mgms., i. e., 0.31 mgm. per gm. mouse. Survived.
June 1.....	13.50	Thyroid as above.
5.....	14.02	
9.....	13.50	Acetonitrile, 5.40 mgms., i. e., 0.40 mgm. per gm. mouse. Died 1½ hours.
June 1.....	16.74	Thyroid as above.
5.....	16.95	
9.....	17.02	Acetonitrile, 9.36 mgms., i. e., 0.55 mgm. per gm. mouse. Died 4 hours.

B. THYROID OF AODAD; IODINE FREE.

1908.		
June 1.....	18.94	Feeding of cakes each containing 0.01 gm. thyroid begun.
5.....	18.52	
9.....	16.52	
10.....		Acetonitrile, 3.63 mgms., i. e., 0.22 mgm. per gm. mouse. Died 2 hours.
June 1.....	24.32	Thyroid as above.
5.....	23.39	
9.....	23.46	
10.....		Acetonitrile, 6.57 mgms., i. e., 0.28 mgm. per gm. mouse. Died 1½ hours.
June 1.....	17.17	Thyroid as above.
5.....	16.86	
9.....	16.66	Acetonitrile, 8.33 mgms., i. e., 0.50 mgm. per gm. mouse. Died 1½ hours.

C. THYROID OF BLACK LEOPARD; 0.01 PER CENT IODINE.

1908.		
June 1.....	15.54	Feeding of cakes each containing 0.01 gm. thyroid begun.
5.....	14.70	
9.....	15.14	Acetonitrile, 5.30 mgms., i. e., 0.35 mgm. per gm. mouse. Survived.
June 1.....	16.72	Thyroid as above.
5.....	15.07	
9.....	13.18	
10.....		Acetonitrile, 5.27 mgms., i. e., 0.40 mgm. per gm. mouse. Died 2½ hours.
June 1.....	17.44	Thyroid as above.
5.....	16.07	
9.....	15.87	
10.....		Acetonitrile, 7.14 mgms., i. e., 0.45 mgm. per gm. mouse. Died 2½ hours.
June 1.....	19.12	Thyroid as above.
5.....	17.72	
9.....	18.33	Acetonitrile, 10.08 mgms., i. e., 0.55 mgm. per gm. mouse. Died 1½ hours.

D. THYROID OF CAT; 0.08 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
June 1.....	16.56	Feeding of cakes each containing 0.001 gm. thyroid begun.
5.....	15.05	
9.....	14.00	Acetonitrile, 7 mgms., i e., 0.5 mgm. per gm. mouse. Survived.
June 1.....	14.08	Thyroid as above.
5.....	14.34	
9.....	14.44	Acetonitrile, 10.11 mgms., i e., 0.7 mgm. per gm. mouse. Survived.
June 1.....	19.29	Thyroid as above.
5.....	18.34	
9.....	17.86	
10.....		Acetonitrile, 15.18 mgms., i e., 0.85 mgm. per gm. mouse. Died 1½ hours.
June 1.....	17.29	Thyroid as above.
5.....	16.50	
9.....	15.68	
10.....		Acetonitrile, 15.68 mgms., i e., 1 mgm. per gm. mouse. Died 2 hours.

E. THYRADEN; 0.085 PER CENT IODINE.

1908.		
June 1.....	14.18	Feeding of cakes each containing 0.001 gm. thyraden begun.
5.....	12.25	
9.....	11.88	Acetonitrile, 8.39 mgms., i e., 0.7 mgm. per gm. mouse. Survived.
June 1.....	17.04	Thyraden as above.
5.....	16.22	
9.....	14.78	Acetonitrile, 11.23 mgms., i e., 0.76 mgm. per gm. mouse. Survived.
June 1.....	16.02	Thyraden as above.
5.....	15.56	
9.....	15.94	
10.....		Acetonitrile, 13.55 mgms., i e., 0.85 mgm. per gm. mouse. Died 3¼ hours.
June 1.....	24.70	Thyraden as above.
5.....	23.58	
9.....	22.50	Acetonitrile, 22.50 mgms., i e., 1 mgm. per gm. mouse. Died 4 hours.

F. THYROID OF DEER; 0.193 PER CENT IODINE.

1908.		
June 1.....	18.82	Feeding of cakes each containing 0.001 gm. thyroid begun.
5.....	17.70	
9.....	16.60	Acetonitrile, 8.30 mgms., i e., 0.5 mgm. per gm. mouse. Survived.
June 1.....	16.16	Thyroid as above.
5.....	14.50	
9.....	15.30	Acetonitrile, 10.71 mgms., i e., 0.7 mgm. per gm. mouse. Survived.
June 1.....	16.34	Thyroid as above.
5.....	14.60	
9.....	15.14	
10.....		Acetonitrile, 13.63 mgms., i e., 0.9 mgm. per gm. mouse. Survived.
June 1.....	17.67	Thyroid as above.
5.....	15.30	
9.....	15.54	
10.....		Acetonitrile, 20.20 mgms., i e., 1.3 mgms., per gm. mouse. Survived.

G. CONTROLS.

Date.	Weight of mouse.	Remarks.
1908.		
June 1.....	15.38	Feeding of cakes without thyroid begun.
5.....	15.10	
9.....	13.92	Acetonitrile, 2.09 mgms., i. e., 0.15 mgm. per gm. mouse. Survived.
June 1.....	16.14	Cakes as above.
5.....	15.42	
9.....	15.30	
11.....	15.92	Acetonitrile, 2.55 mgms., i. e., 0.16 mgm. per gm. mouse. Survived.
June 1.....	16.42	Cakes as above.
5.....	16.86	
9.....	15.72	
10.....		Acetonitrile, 2.67 mgms., i. e., 0.17 mgm. per gm. mouse. Survived.
June 1.....	23.34	Cakes as above.
5.....	21.88	
9.....	21.45	
10.....		Acetonitrile, 3.86 mgms., i. e., 0.18 mgm. per gm. mouse. Died 1 hour.
June 1.....	17.02	Cakes as above.
5.....	16.00	
9.....	14.78	
10.....		Acetonitrile, 2.81 mgms., i. e., 0.19 mgm. per gm. mouse. Died 4½ hours.
June 1.....	18.30	Cakes as above.
5.....	18.42	
9.....	17.66	Acetonitrile, 3.53 mgms., i. e., 0.20 mgm. per gm. mouse. Died 1¼ hours.

Summary.—The results of the above experiments may be tabulated as follows:

Thyroid.	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgm. per gm. mouse.	
				Recovered.	Died.
A. Alaskan bear.....	0.01	0	0	0.31	0.40
B. Aoudad.....	.01	0	022
C. Black leopard.....	.01	.01	.001	.35	.40
D. Cat.....	.001	.08	.0008	.70	.85
E. Thyraden.....	.001	.085	.00085	.76	.85
F. Deer.....	.001	.193	.00193	1.30
G. Controls.....				.17	.18

The thyroid of the Alaskan bear (A) had a low degree of physiological activity. Inasmuch as 0.01 gm. (per cake) protected against only about one-half as much acetonitrile as did 0.001 of thyraden (0.085 per cent iodine), we may estimate the physiological activity of the latter to be approximately twenty times as great as that of the former. If the aoudad thyroid (B) had any physiological activity, it was too slight to be demonstrated by these experiments; in any case, it was distinctly weaker than the Alaskan bear thyroid (A). The thyroid of the black leopard (C) with 0.01 per cent iodine was apparently no more active than the iodine free thyroid of the Alaskan

bear. The experiments with the cat (D) and deer (F) thyroids show that there is a direct parallelism between the iodine content and the physiological activity of thyroid.

SUMMARY AND GENERAL CONCLUSIONS.

The above experiments show that iodine free thyroid, or what is usually called "iodine free" thyroid, has, when tested by our method, a low degree of physiological activity; this result is contrary to that reported by others. The experiments also show that the activity of such thyroid is much less than that of thyroid containing more than distinct traces (0.01 per cent, for example) of iodine. It is also evident that there are differences in the activity of different "iodine free" thyroids; those of the Alaskan bear and of children were more active than those of the Maltese kid or of the aoudad. This may be explained on either of two suppositions: it may be assumed that the activity of the so-called "iodine free" thyroid is in reality due to iodine which is present in too small amounts to be detected when only small samples are available for analysis and that there is more iodine in the thyroids of the children and of the Alaskan bear than in those of the Maltese kid and of the aoudad. Or we may suppose that the iodine free thyreoglobulin has of itself some activity and that the greater activity of some of the "iodine free" thyroids is due to their containing a larger amount of this thyreoglobulin than do other thyroids. This suggestion would also explain why certain "iodine free" thyroids (children and Alaskan bear) are more active than thyroid (black leopard) containing a minimum amount of iodine. The effect of a large amount of iodine free thyreoglobulin may be greater than that of a small amount of iodine containing thyreoglobulin. In connection with this suggestion attention may be called to the work of Oswald,^a in which it is shown that the thyreoglobulin varies greatly in amount in different thyroids.

Evidence will be presented in later parts of this bulletin that the physiological activity of the thyroid increases in direct proportion to the amount of iodine contained in proper combination. Some of the bearings (upon the physiology and pathology of the thyroid) of this view that iodine free thyroid has a certain degree of activity and that this is much increased by the presence, in proper combination, of iodine have been discussed by one of the present writers in a previous paper.^b Another application of this conception may be referred to, although it is not our purpose to discuss fully in this connection these collateral subjects. It was stated in the historical review (p. 13) that one of the arguments advanced against the view

^a A. Oswald, Beitr. z. chem. Physiol. u. Path., Brnschw., 1902, 2, p. 545.

^b R. Hunt, J. Am. M. Ass., Chicago, 1907, 49, p. 1325.

that iodine (or rather an iodine containing substance) is an important constituent of the thyroid was the fact that the removal of thyroids which contain no iodine is followed by as severe symptoms as the removal of those which do contain iodine. Such a result would be inexplicable on the view that an iodine compound is an essential constituent of the thyroid; it would, however, be intelligible on the hypothesis that thyroid free of iodine alone has a certain degree of physiological activity. We may suppose that this iodine free or iodine poor thyreoglobulin is sufficient, as a rule, for the ordinary purposes of the organism. Much of the iodine usually found in the thyroid may be considered as one of those "factors of safety" discussed by Meltzer.^a That the iodine free or iodine poor thyreoglobulin is not, however, always adequate to meet the demands of the body is shown, for example, by the losses suffered by sheep breeders on account of cretin lambs before the extensive use of iodine containing salt.^b

Another indication that the iodine serves a useful purpose is that there is in general an inverse ratio between the size of the thyroid and the amount of iodine it contains.

ii. COMPARATIVE PHYSIOLOGICAL ACTIVITY OF COMMERCIAL SHEEP THYROIDS.

Inasmuch as most of the commercial thyroid preparations are obtained from the sheep, and as these are official in the United States and several other pharmacopœias, especial attention was given to the comparison of their iodine content and physiological activity. There is a widespread belief among clinicians that commercial thyroid preparations differ considerably in activity; we believe that this opinion is fully justified.

Before describing the results of our experiments a few remarks may be made as to the character of quantitative results which may be expected in a study of the physiological action of drugs. When the great importance, both theoretical and practical, of dosage in medicine is considered, it is remarkable that so little work has been done on the scientific principles underlying it.^c Not many physicians would assume that by doubling the dose of a drug twice the effect would be produced, yet the relation between successive increments of the dose and the physiological effects is unknown in the case of nearly all drugs. With some drugs, in certain doses, double the amount will produce twice the physiological effect. In other

^a S. J. Meltzer, *J. Am. M. Ass.*, Chicago, 1907, **48**, p. 655.

^b *cf.* D. Marine, *Johns Hopkins Hosp. Bull.*, 1907, **18**, p. 359.

^c *cf.* Juckuff, *Versuche zur Auffindung eines Dosierungsgesetztes*, Leipzig, 1895; E. Harnack, *München med. Wchnschr.*, 1896, **43**, p. 1065; J. T. Cash, *Brit. Med. J.*, Lond., 1908, i, p. 1213.

doses an increase of 10 per cent in the amount may produce twice the effect. With still other doses the amount administered may be increased many times before twice the effect is produced.

The relation between the percentage of iodine in thyroid and its activity in increasing the resistance of mice to acetonitrile seems to offer an unusually favorable opportunity for a study of this character, but we have not been able to devote special attention to it. A brief discussion of the subject is, however, indispensable for an understanding of our results and the conclusions we draw from them. From the experiments already described (Series II, children's thyroids, p. 35) it is evident that even a very weak thyroid preparation will, when given in a sufficient dose, produce as great a physiological effect as an equal amount of a very active preparation. In other words, there is a limit to the degree of resistance which the body can acquire even under the most favorable circumstances. It is obviously necessary, in comparing the physiological effects of different thyroid preparations, to avoid doses which produce a maximum effect. Also, as the doses approach the maximum, each successive increase produces a relatively smaller effect. A curve expressing these facts graphically is a parabola; at a certain point a preparation with twice the activity of another will produce twice the effect; one with three times the activity would produce three times the effect, etc. The farther removed the doses are from this optimum the less close is the correspondence between the size of the dose of the preparation and its (measurable) physiological effect. The range through which there is a direct relation between the physiological activity of the thyroid and the amount of acetonitrile which may be rendered harmless under its influence seems to be rather great; this doubtlessly accounts for the comparative ease with which we have obtained quantitative results in the following experiments.

In work of this character it is not only permissible but necessary to exclude experiments in which the thyroid produced maximum effects. Thus it would obviously be unwarranted to conclude from the experiments of Series II (p. 35) that the thyroid of children is as active as that of sheep because 0.05 gm. of the former protected against as much acetonitrile as did 0.05 gm. of the latter; in each case the amount fed was probably far above that necessary to produce the maximum effect.

The plan of our experiments was as follows: When the activity of several thyroid preparations was to be compared, they were fed in equal amounts, but care was taken that the quantities administered were such as we believed would produce submaximum effects. It was sometimes necessary to perform two or three series of experiments of this character before the amounts most suitable for comparison could be determined; this was partly due to the fact that

different lots of mice reacted differently. Thus with some mice 0.001 gm. each of several thyroid preparations produced a maximum effect; in such a case it was necessary to repeat the experiments using 0.0005 gm. for example. In other cases the physiological effects produced by the feeding of 0.001 gm. of different thyroid preparations were very slight; in such cases the experiments were repeated with 0.002 or more gram. When the experiments were performed in this manner we found that the amount of acetonitrile from which the mice recovered under the influence of the thyroid was almost directly proportional to the amount of iodine the thyroid contained; hence we conclude that the physiological activity of thyroid is proportional to the iodine content. The correctness of this conclusion was often confirmed as follows: If it required twice as much acetonitrile to cause the death of mice to which thyroid A had been fed as of those to which an equal amount of thyroid B had been fed, we found that the fatal dose of the nitrile was about the same in each case when two parts of B on the one hand and one part of A on the other were fed.^a Results of greater scientific accuracy could probably have been obtained by a slightly different method of experimenting. Thus instead of comparing the total amount of thyroid which produced a given degree of protection, it would probably have been more accurate to first subtract the "maximum ineffective" dose (i. e., the maximum amount of thyroid which could be fed without producing any demonstrable physiological effect) ^b and comparing only the amounts in excess of this dose. Similarly it would have probably been more accurate to subtract from the maximum nonlethal doses of the nitrile the maximum doses from which the mice would have recovered had they received no thyroid. In this way the amounts of the poison actually neutralized under the influence of the thyroid would have been compared. Such refinements of experimentation were, however, not necessary for our purpose, which was simply to determine if there is a parallelism between the iodine content and the physiological activity of the thyroid

It may be well to emphasize again some of the precautions necessary in this work. One of the most important of these is to have mice which have been kept under uniform conditions; the susceptibility of different lots of mice may vary widely even at the same season. Hence it is necessary to have a number of controls for each series of experiments. It is also necessary to work with doses which are not too near either the minimum or the maximum.

^a This method of double control is similar to the one adopted by one of us in comparing the physiological activity of suprarenal preparations. (J. Am. M. Ass., 1906, 47, p. 790.)

^b cf. J. T. Cash, Brit. M. J., Lond., 1908, i, p. 1213.

Great care is also required in making the cakes. In some of our experiments we have worked with 1 part of thyroid mixed with 40,000 parts of cracker dust. It is obvious that a uniform distribution of such a small amount of thyroid in such a large amount of cracker dust by ordinary laboratory methods requires considerable care. That, however, remarkably concordant results may be obtained by this method is sufficiently demonstrated by the experiments which follow.

SERIES I.

A. SHEEP THYROID; 0.087 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
November 22...	22.63	Feeding of cakes each containing 0.005 gm. thyroid commenced.
26...	22.45	
29...	21.62	
December 2...	21.52	Acetonitrile, 38.74 mgms., i. e., 1.8 mgms. per gm. mouse. Survived.
November 22...	16.32	Thyroid as above.
26...	16.42	
29...	16.59	
December 2...	16.07	Acetonitrile, 32.64 mgms., i. e., 2 mgms. per gm. mouse. Died 1½ hours.
3...	16.32	
November 22...	20.39	Thyroid as above.
26...	19.44	
29...	19.10	
December 2...	18.59	Acetonitrile, 41.5 mgms., i. e., 2.2 mgms. per gm. mouse. Died 2 hours.
3...	18.87	
November 22...	21.79	Thyroid as above.
26...	21.57	
29...	20.70	
December 2...	19.63	Acetonitrile, 45.65 mgms., i. e., 2.5 mgms. per gm. mouse. Died 1 hour.
3...	18.26	

B. SHEEP THYROID; 0.17 PER CENT IODINE.

1907.		
November 22...	18.52	Feeding of cakes each containing 0.005 gm. thyroid begun.
26...	18.35	
29...	18.33	
December 2...	17.04	Acetonitrile, 34.1 mgms., i. e., 2 mgms. per gm. mouse. Survived.
November 22...	22.92	Thyroid as above.
26...	21.00	
29...	21.65	
December 2...	20.64	Acetonitrile, 57.79 mgms., i. e., 2.8 mgms. per gm. mouse. Survived.
November 22...	16.00	Thyroid as above.
26...	16.39	
29...	16.56	
December 2...	16.70	Acetonitrile, 55.09 mgms., i. e., 3.5 mgms. per gm. mouse. Survived.
3...	15.74	
November 22...	20.28	Thyroid as above.
26...	18.41	
29...	18.35	
December 2...	17.48	Acetonitrile, 78.3 mgms., i. e., 4 mgms. per gm. mouse. Died ¾ hour.
3...	17.08	

C. CONTROLS.

Date.	Weight of mouse.	Remarks.
1907.		
November 22...	20.03	Feeding of cakes without thyroid begun.
26...	20.17	
29...	19.85	
December 2...	19.30	Acetonitrile, 7.33 mgms., i. e., 0.38 mgm. per gm. mouse. Survived.
November 22...	21.38	Cakes as above.
26...	20.00	
29...	20.26	
December 2...	19.07	Acetonitrile, 8.11 mgms., i. e., 0.43 mgm. per gm. mouse. Survived.
3...	18.86	
November 22...	22.67	Cakes as above.
26...	20.40	
29...	19.44	
December 2...	19.30	Acetonitrile, 8.69 mgms., i. e., 0.45 mgm. per gm. mouse. Died 4 hours.
November 22...	23.63	Cakes as above.
26...	22.89	
29...	21.65	
December 2...	21.96	
3...	22.32	
4...	22.43	Acetonitrile, 10.54 mgms., i. e., 0.47 mgm. per gm. mouse. Died 2 hours.

Summary.—The results of the above experiments may be summarized as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.005	0.087	0.00435	1.8	2.0
B.....	.005	.170	.0085	3.5	4.0
C. Controls.....				.43	.45

The thyroid with approximately twice the amount of iodine protected against approximately twice the dose of acetonitrile.

SERIES II.

The same thyroid preparations as above were used, but twice as much of the iodine poor as of the iodine rich was given. The experiments were performed upon a different lot of mice.

A. SHEEP THYROID; 0.17 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
December 5...	16.00	Feeding of cakes each containing 0.002 gm. thyroid begun.
9...	15.67	
12...	16.28	
14...	15.72	
15...	15.80	Acetonitrile, 33.18 mgms., i. e., 2.1 mgms. per gm. mouse. Survived.
December 5...	17.54	Thyroid as above.
9...	18.06	
12...	18.13	
14...	17.91	
15...	17.57	Acetonitrile, 40.41 mgms., i. e., 2.3 mgms. per gm. mouse. Survived.
December 5...	20.08	Thyroid as above.
9...	21.20	
12...	20.92	
14...	20.65	Acetonitrile, 49.56 mgms., i. e., 2.4 mgms. per gm. mouse. Died 2 to 3 hours.
December 5...	15.37	Thyroid as above.
9...	15.16	
12...	15.36	
14...	16.31	Acetonitrile, 48.93 mgms., i. e., 3 mgms. per gm. mouse. Died 5½ hours.

B. SHEEP THYROID; 0.087 PER CENT IODINE.

1907.		
December 5...	14.00	Feeding of cakes each containing 0.004 gm. thyroid begun.
9...	14.92	
12...	14.42	
14...	14.76	
15...	14.05	Acetonitrile, 28.1 mgms., i. e., 2 mgms. per gm. mouse. Survived.
December 5...	15.17	Thyroid as above.
9...	15.49	
12...	15.37	
14...	15.22	
15...	14.28	Acetonitrile, 32.84 mgms., i. e., 2.3 mgms. per gm. mouse. Survived.
December 5...	16.41	Thyroid as above.
9...	16.59	
12...	16.46	
14...	16.54	
15...	16.30	Acetonitrile, 40.75 mgms., i. e., 2.5 mgms. per gm. mouse. Died 2 hours.
December 5...	19.38	Thyroid as above.
9...	20.86	
12...	21.76	
14...	21.46	Acetonitrile, 60.09 mgms., i. e., 2.8 mgms. per gm. mouse. Died 3½ hours.

C. CONTROLS.^a

Date.	Weight of mouse.	Remarks.
1907.		
December 5...	17.55	Feeding of cakes without thyroid begun.
9...	17.38	
12...	17.54	
14...	17.93	
15...	17.80	Acetonitrile, 3.03 mgms., i. e., 0.17 mgm. per gm. mouse. Survived.
December 5...	15.33	Cakes as above.
9...	15.88	
12...	16.25	
14...	16.52	
15...	15.97	Acetonitrile, 3.03 mgms., i. e., 0.19 mgm. per gm. mouse. Died 1½ hours.
December 5...	17.31	Cakes as above.
9...	17.91	
12...	17.53	
14...	18.12	Acetonitrile, 3.81 mgms., i. e., 0.21 mgm. per gm. mouse. Died 2½ hours.
December 5...	15.09	Cakes as above.
9...	15.24	
12...	14.85	
14...	15.06	Acetonitrile, 3.77 mgms., i. e., 0.25 mgm. per gm. mouse. Died 6¼ hours.

^a It will be noticed that the fatal dose of acetonitrile for the mice of this series was less than one-half as large as that for those of the preceding series. Such variations in susceptibility are frequent and are largely the result of diet, differences in age, weight, etc.; it illustrates the necessity for using only those mice which have been kept under identical conditions and also the necessity for many controls.

Summary.—The results of the above experiments may be summarized as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.004	0.087	0.00348	2.3	2.5
B.....	.002	.17	.0034	2.3	2.4
C. Controls.....				.17	.19

When two parts of A (0.087 per cent iodine) and one part of B (0.17 per cent iodine) were fed, equal physiological effects were produced.

SERIES III.

In this series both of the methods referred to above were employed, i. e., equal amounts of thyroid containing different amounts of iodine and different amounts of thyroid containing equal amounts of iodine were given. Unfortunately we are not absolutely certain that the analytical data are entirely correct for one of the preparations, viz, that stated to contain 0.061 per cent of iodine. This was the figure obtained on the analysis of a sample taken from the surface of the bottle; later analyses of the thoroughly mixed contents of the bottle showed 0.1 per cent iodine. Inasmuch as the physiological activity of the surface layer corresponded to that of thyroid

containing about 0.061 per cent iodine, and as we have often found that the percentage of iodine in a sample of thyroid can be fairly accurately determined by these physiological tests, we are inclined to believe the analysis correct. Even supposing that the thyroid used contained 0.1 per cent iodine, the results show that there is at least a general parallelism between the iodine content and the physiological activity of the thyroid.

A. SHEEP THYROID; 0.061 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
November 28...	15.97	Feeding of cakes, each containing 0.002 gm. thyroid, commenced.
30...	15.66	
December 3...	15.45	Acetonitrile, 13.73 mgms., i. e., 0.9 mgm. per gm. mouse. Survived.
6...	15.36	
7...	15.25	
November 28...	18.04	Thyroid as above.
30...	17.82	
December 3...	17.63	Acetonitrile, 19.1 mgms., i. e., 1.1 mgms. per gm. mouse. Survived.
6...	17.19	
8...	17.36	
November 28...	19.99	Thyroid as above.
30...	20.39	
December 3...	21.38	Acetonitrile, 24.77 mgms., i. e., 1.2 mgms. per gm. mouse. Died, 3 hours.
6...	20.59	
7...	20.64	
November 28...	18.89	Thyroid as above.
30...	18.08	
December 3...	17.93	Acetonitrile, 23.24 mgms., i. e., 1.3 mgms. per gm. mouse. Died, 1 hour.
6...	17.52	
8...	17.88	

B. SHEEP THYROID; 0.061 PER CENT IODINE.

1907.		
November 28...	16.32	Feeding of cakes, each containing 0.006 gm. thyroid, commenced.
30...	16.24	
December 3...	15.77	Acetonitrile, 23.58 mgms., i. e., 1.5 mgms. per gm. mouse. Survived.
6...	15.52	
7...	15.72	
November 28...	15.06	Thyroid as above.
30...	13.35	
December 3...	13.50	Acetonitrile, 32.64 mgms., i. e., 2.4 mgms. per gm. mouse. Survived.
6...	13.23	
7...	13.60	
November 28...	17.62	Thyroid as above.
30...	17.46	
December 3...	18.06	Acetonitrile, 59.06 mgms., i. e., 3.1 mgms. per gm. mouse. Survived.
6...	17.78	
8...	19.05	
November 28...	21.43	Thyroid as above.
30...	20.97	
December 3...	20.13	Acetonitrile, 69.55 mgms., i. e., 3.6 mgms. per gm. mouse. Died, three-fourths hour.
6...	19.53	
8...	19.32	

C. SHEEP THYROID: 0.192 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
November 28...	18.07	Feeding of cakes, each containing 0.002 gm. thyroid, commenced.
30...	17.85	
December 3...	17.50	
6...	16.77	
7...	17.24	Acetonitrile, 37.93 mgms., i. e., 2.2 mgms. per gm. mouse. Survived.
November 28...	16.00	Thyroid as above.
30...	16.85	
December 3...	16.07	
6...	15.47	
7...	14.92	Acetonitrile, 41.78 mgms., i. e., 2.8 mgms. per gm. mouse. Survived.
November 28...	21.85	Thyroid as above.
30...	20.05	
December 3...	22.40	
6...	20.62	
8...	21.16	Acetonitrile, 69.83 mgms., i. e., 3.3 mgms. per gm. mouse. Survived.
November 28...	17.67	Thyroid as above.
30...	15.59	
December 3...	16.07	
6...	16.17	
8...	15.71	Acetonitrile, 58.13 mgms., i. e., 3.7 mgms. per gm. mouse. Died, one-half hour.

D. CONTROLS.

1907.		
November 28...	21.77	Feeding of cakes without thyroid begun.
30...	21.92	
December 3...	21.09	
6...	20.78	
8...	20.57	Acetonitrile, 5.14 mgms., i. e., 0.25 mgm. per gm. mouse. Died, about 2 hours.
November 28...	24.50	Cakes as above.
30...	23.96	
December 3...	24.51	
6...	24.32	
8...	24.51	Acetonitrile, 7.35 mgms., i. e., 0.3 mgm. per gm. mouse. Died 1½ hours.
November 28...	21.86	Cakes as above.
30...	21.50	
December 3...	21.52	
6...	20.74	
8...	21.50	Acetonitrile, 7.53 mgms., i. e., 0.35 mgm. per gm. mouse. Died 3 hours.

Summary.—The results of the above experiments may be summarized as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.002	0.061	0.00122	1.1	1.2
B.....	.006	.061	.00366	3.1	3.6
C.....	.002	.192	.00384	3.3	3.7
D. Controls.....					.25

Two thousandths of a gram of thyroid containing 0.192 per cent iodine protected mice against as much acetonitrile as did 0.006 gm. thyroid containing but 0.061 per cent iodine.

Further, with equal amounts of the two thyroid preparations, that containing 0.192 per cent iodine protected against three times as much acetonitrile as did that containing but 0.061 per cent iodine.

SERIES IV.

A. SHEEP THYROID; 0.1 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
January 15.....	25.65	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
18.....	26.80	
21.....	26.52	
24.....	26.50	
26.....	26.50	
		Acetonitrile, 37.1 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.
January 15.....	21.47	Thyroid as above.
18.....	22.05	
21.....	21.36	Acetonitrile, 30 mgms., i. e., 1.5 mgms. per gm. mouse. Survived.
24.....	20.00	
January 15.....	27.50	Thyroid as above.
18.....	27.88	
21.....	27.92	Acetonitrile, 43.35 mgms., i. e., 1.7 mgms. per gm. mouse. Died, 1½ hours.
24.....	27.88	
25.....	25.50	
January 15.....	22.38	Thyroid as above.
18.....	23.56	
21.....	22.35	Acetonitrile, 44.04 mgms., i. e., 2 mgms. per gm. mouse. Died, 2 hours.
24.....	22.22	
25.....	22.02	

B. SHEEP THYROID; 0.19 PER CENT IODINE.

1908.		
January 15.....	27.74	Feeding of cakes each containing 0.001 gm. thyroid commenced.
18.....	27.32	
21.....	27.43	
24.....	26.70	
		Acetonitrile, 53.4 mgms., i. e., 2 mgms. per gm. mouse. Survived.
January 15.....	20.88	Thyroid as above.
18.....	22.50	
21.....	22.45	Acetonitrile, 54.75 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
24.....	21.58	
25.....	21.90	
January 15.....	19.30	Thyroid as above.
18.....	19.42	
21.....	18.58	Acetonitrile, 51.98 mgms., i. e., 2.7 mgms. per gm. mouse. Survived.
24.....	18.58	
26.....	19.25	
January 15.....	21.52	Thyroid as above.
18.....	20.91	
21.....	21.22	Acetonitrile, 62.79 mgms., i. e., 3 mgms. per gm. mouse. Died 1 hour.
24.....	20.69	
26.....	20.93	

C. SHEEP THYROID; 0.1 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
January 15.....	20.00	Feeding of cakes each containing 0.005 gm. thyroid commenced.
18.....	20.30	
21.....	20.27	
24.....	19.70	Acetonitrile, 68.95 mgms., i. e., 3.5 mgms. per gm. mouse. Survived.
January 15.....	22.52	Thyroid as above.
18.....	21.51	
21.....	21.36	
24.....	20.72	
25.....	21.21	Acetonitrile, 95.45 mgms., i. e., 4.5 mgms. per gm. mouse. Survived.
January 15.....	22.72	Thyroid as above.
18.....	22.98	
21.....	22.50	
24.....	22.22	
26.....	21.75	Acetonitrile, 108.75 mgms., i. e., 5 mgms. per gm. mouse. Died 1½ hours.
January 15.....	21.55	Thyroid as above.
18.....	22.58	
21.....	22.68	
24.....	22.70	
26.....	22.50	Acetonitrile, 123.75 mgms., i. e., 5.5 mgms. per gm. mouse. Died 2½ hours.

D. SHEEP THYROID; 0.19 PER CENT IODINE.

1908.		
January 15.....	23.13	Feeding of cakes each containing 0.005 gm. thyroid commenced.
18.....	21.30	
21.....	22.12	
24.....	21.06	Acetonitrile, 84.24 mgms., i. e., 4 mgms. per gm. mouse. Survived.
January 15.....	24.17	Thyroid as above.
18.....	25.28	
21.....	24.44	
24.....	23.40	
26.....	24.25	Acetonitrile, 133.38 mgms., i. e., 5.5 mgms. per gm. mouse. Died 2 hours.
January 15.....	21.67	Thyroid as above.
18.....	21.80	
21.....	20.90	
24.....	19.62	
26.....	19.38	Acetonitrile, 116.3 mgms., i. e., 6 mgms. per gm. mouse. Died 5 hours.

The experiments on the controls for this series were somewhat irregular, but the fatal dose was apparently between 0.4 and 0.5 mg. acetonitrile per gram mouse.

SUMMARY.

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.001	0.1	0.001	1.4	1.7
B.....	.001	.19	.0019	2.7	3.0
C.....	.005	.1	.005	4.5	5.0
D.....	.005	.19	.0095	4.0	5.5
Controls.....				.4(?)	.5(?)

From A and B it is seen that the thyroid containing 0.19 per cent iodine was nearly twice as active as that containing 0.1 per cent. In C and D the effects (with 0.005 gm. thyroid in each cake) were apparently maximum in each case, so that no difference in the activity of the two preparations was apparent.

SERIES V.

A series very similar to the above is the following:

A. SHEEP THYROID; 0.1 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
February 11....	22.99	Feeding of cakes each containing 0.001 gm. thyroid commenced.
14....	21.66	
17....	22.07	
20....	21.61	
21....	21.74	Acetonitrile, 34.78 mgms., i. e., 1.6 mgms. per gm. mouse. Survived.
February 11....	23.06	Thyroid as above.
14....	21.13	
17....	21.76	
20....	20.94	
21....	21.77	Acetonitrile, 45.72 mgms., i. e., 2.1 mgms. per gm. mouse. Died 2½ hours.
February 11....	18.50	Thyroid as above.
14....	17.79	
17....	17.47	
20....	17.43	Acetonitrile, 43.58 mgms., i. e., 2.5 mgms. per gm. mouse. Died 3½ hours.
February 11....	20.14	Thyroid as above.
14....	17.48	
17....	17.81	
20....	17.45	Acetonitrile, 52.35 mgms., i. e., 3 mgms. per gm. mouse. Died 2½ hours.

B. SHEEP THYROID; 0.19 PER CENT IODINE.

1908.		
February 11....	16.80	Feeding of cakes each containing 0.001 gm. thyroid commenced.
14....	16.02	
17....	16.41	
20....	17.10	Acetonitrile, 34.2 mgms., i. e., 2 mgms. per gm. mouse. Survived.
February 11....	21.25	Thyroid as above.
14....	20.90	
17....	22.48	
20....	17.13	Acetonitrile, 42.83 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
February 11....	16.38	Thyroid as above
14....	15.29	
17....	15.09	
20....	15.17	
21....	15.59	Acetonitrile, 46.77 mgms., i. e., 3 mgms. per gm. mouse. Survived.
February 11....	21.69	Thyroid as above.
14....	20.46	
17....	21.02	
20....	20.64	
21....	20.90	Acetonitrile, 73.15 mgms., i. e., 3.5 mgms. per gm. mouse. Died 1½ hours.

C. CONTROLS.

Date.	Weight of mouse.	Remarks.
1908.		
February 11....	13.98	Feeding of cakes without thyroid commenced.
14....	13.91	
17....	14.26	
20....	13.75	
21....	14.33	Acetonitrile, 4.59 mgms., i. e., 0.32 mgm. per gm. mouse. Survived.
February 11....	19.48	Cakes as above.
14....	17.70	
17....	17.45	
20....	16.90	
21....	17.42	Acetonitrile, 6.62 mgms., i. e., 0.38 mgm. per gm. mouse. Survived.
February 11....	14.98	Cakes as above.
14....	13.08	
17....	12.72	
20....	12.85	
21....	13.04	Acetonitrile, 7.17 mgms., i. e., 0.55 mgm. per gm. mouse. Died 4½ hours.

Summary.—The results of the above experiments may be summarized as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgm. per gm.	
				Recovered.	Died.
A.....	0.001	0.1	0.0010	1.6	2.1
B.....	.001	.19	.0019	3.0	3.5
C. Controls.....				.38	.55

SERIES VI.

In this series the effects of a number of commercial thyroid powders with different percentages of iodine were compared; the effects of different amounts were also compared.

A. SHEEP THYROID; 0.11 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
April 8.....	13.41	Feeding of cakes each containing 0.001 gm. thyroid commenced.
11.....	12.68	
14.....	13.32	
16.....	13.25	
		Acetonitrile, 26.50 mgms., i. e., 2 mgms. per gm. mouse. Survived
April 8.....	12.82	Thyroid as above.
11.....	12.30	
14.....	13.26	
16.....	13.22	
17.....	13.13	Acetonitrile, 32.83 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
April 8.....	14.63	Thyroid as above.
11.....	14.72	
14.....	14.06	
16.....	13.54	
17.....	13.22	Acetonitrile, 39.66 mgms., i. e., 3 mgms. per gm. mouse. Died 10 hours.
April 8.....	13.17	Thyroid as above.
11.....	13.50	
14.....	12.90	
17.....	13.02	Acetonitrile, 45.57 mgms., i. e., 3.5 mgms. per gm. mouse. Died 1½ hours.

A¹. SAME PREPARATION AS ABOVE.

Date.	Weight of mouse.	Remarks.
1908.		
April 8.....	14.30	Feeding of cakes each containing 0.002 gm. thyroid commenced.
11.....	14.96	
14.....	14.67	
16.....	14.20	Acetonitrile, 53.96 mgms., i. e., 3.8 mgms. per gm. mouse. Survived.
April 8.....	12.31	Thyroid as above.
11.....	12.44	
14.....	12.43	
16.....	12.42	
17.....	12.39	Acetonitrile, 50.8 mgms., i. e., 4.1 mgms. per gm. mouse. Survived.
April 8.....	13.21	Thyroid as above.
11.....	13.12	
14.....	13.50	
17.....	13.40	Acetonitrile, 61.64 mgms., i. e., 4.6 mgms. per gm. mouse. Died three-fourths hour.

B. SHEEP THYROID; 0.13 PER CENT IODINE.

1908.		
April 8.....	18.14	Feeding of cakes each containing 0.001 gm. thyroid commenced.
11.....	19.19	
14.....	17.07	
16.....	17.00	Acetonitrile, 37.4 mgms., i. e., 2.2 mgms. per gm. mouse. Survived.
April 8.....	17.64	Thyroid as above.
11.....	19.36	
14.....	20.48	
16.....	20.43	
17.....	20.50	Acetonitrile, 49.2 mgms., i. e., 2.4 mgms. per gm. mouse. Survived.
April 8.....	16.08	Thyroid as above.
11.....	17.31	
14.....	17.15	
16.....	17.86	Acetonitrile, 48.22 mgms., i. e., 2.7 mgms. per gm. mouse. Died 4 hours.
April 8.....	12.34	Thyroid as above.
11.....	13.17	
14.....	12.86	
17.....	12.82	Acetonitrile, 35.9 mgms., i. e., 2.8 mgms. per gm. mouse. Survived.

C. SHEEP THYROID; 0.13 PER CENT IODINE.

1908.		
April 8.....	15.76	Feeding of cakes each containing 0.001 gm. thyroid commenced.
11.....	15.00	
14.....	14.97	
16.....	15.40	Acetonitrile, 33.88 mgms., i. e., 2.2 mgms. per gm. mouse. Survived.
April 8.....	17.80	Thyroid as above.
11.....	18.24	
14.....	18.09	
16.....	18.16	
17.....	18.23	Acetonitrile, 47.4 mgms., i. e., 2.6 mgms. per gm. mouse. Survived.
April 8.....	19.50	Thyroid as above.
11.....	19.26	
14.....	19.02	
17.....	17.28	
18.....	17.07	Acetonitrile, 49.5 mgms., i. e., 2.9 mgms. per gm. mouse. Survived.
April 8.....	13.20	Thyroid as above.
11.....	13.18	
14.....	12.98	
17.....	16.86	Acetonitrile, 52.27 mgms., i. e., 3.1 mgms. per gm. mouse. Died 1½ hours.

D. SHEEP THYROID; 0.1 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
April 8.....	16.34	Feeding of cakes each containing 0.001 gm. thyroid commenced.
11.....	16.31	
14.....	16.06	
16.....	15.77	Acetonitrile, 36.27 mgms., i. e., 2.3 mgms. per gm. mouse. Survived.
April 8.....	13.50	Thyroid as above.
11.....	14.42	
14.....	14.83	
16.....	14.43	
17.....	14.95	Acetonitrile, 40.38 mgms., i. e., 2.8 mgms. per gm. mouse. Survived.
April 8.....	15.07	Thyroid as above.
11.....	15.76	
14.....	14.47	
17.....	14.22	Acetonitrile, 48.35 mgms., i. e., 3.4 mgms. per gm. mouse. Survived.
April 8.....	14.12	Thyroid as above.
11.....	13.92	
14.....	13.63	
17.....	12.93	
18.....	13.42	Acetonitrile, 50.99 mgms., i. e., 3.8 mgms. per gm. mouse. Survived.

D¹. SAME PREPARATION AS ABOVE.

1908.		
April 8.....	14.88	Feeding cakes each containing 0.002 gm. thyroid commenced.
11.....	15.12	
14.....	14.50	
16.....	14.50	Acetonitrile, 52.2 mgms., i. e., 3.6 mgms. per gm. mouse. Survived.
April 8.....	10.94	Thyroid as above.
11.....	11.30	
14.....	11.48	
17.....	10.83	Acetonitrile, 41.15 mgms., i. e., 3.8 mgms. per gm. mouse. Died about 30 hours.
April 8.....	14.94	Thyroid as above.
11.....	14.82	
14.....	13.39	
17.....	12.88	
18.....	12.13	Acetonitrile, 47.3 mgms., i. e., 3.9 mgms. per gm. mouse. Died 5 hours.
April 8.....	13.05	Thyroid as above.
11.....	13.98	
14.....	14.06	
17.....	13.75	
18.....	13.66	Acetonitrile, 56 mgms., i. e., 4.1 mgms. per gm. mouse. Died 1½ hours.

E. SHEEP THYROID; 0.19 PER CENT IODINE.

1908.		
April 8.....	12.40	Feeding cakes each containing 0.001 gm. thyroid commenced.
11.....	12.70	
14.....	12.37	
16.....	12.26	Acetonitrile, 50.27 mgms., i. e., 4.1 mgms. per gm. mouse. Survived.
April 8.....	13.59	Thyroid as above.
11.....	13.76	
14.....	13.45	
16.....	13.00	
17.....	12.85	Acetonitrile, 56.54 mgms., i. e., 4.4 mgms. per gm. mouse. Survived.
April 8.....	17.55	Thyroid as above.
11.....	18.12	
14.....	18.02	
16.....	19.24	Acetonitrile, 88.5 mgms., i. e., 4.6 mgms. per gm. mouse. Died 1½ hours.
April 8.....	14.74	Thyroid as above.
11.....	14.48	
14.....	14.55	
17.....	14.56	Acetonitrile, 68.43 mgms., i. e., 4.7 mgms. per gm. mouse. Survived.

F. SHEEP THYROID; 0.19 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
April 8.....	12.02	Feeding of cakes each containing 0.001 gm. thyroid commenced.
11.....	12.00	
14.....	11.80	
16.....	11.11	Acetonitrile, 42.22 mgms., i. e., 3.8 mgms. per gm. mouse. Survived.
April 8.....	14.37	Thyroid as above.
11.....	14.08	
14.....	13.74	
16.....	12.90	Acetonitrile, 56.76 mgms., i. e., 4.4 mgms. per gm. mouse. Survived.
April 8.....	13.08	Thyroid as above.
11.....	13.14	
14.....	13.36	
16.....	13.52	
17.....	12.94	Acetonitrile, 62.11 mgms., i. e., 4.8 mgms. per gm. mouse. Died 2½ hours

SUMMARY.

	Gm. thyroid fed daily.	Percent- age of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of aceto- nitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.001	0.11	0.0011	2.5	3.0
A¹.....	.002	.11	.0022	4.1	4.6
B.....	.001	.13	.0013	2.8	2.7
C.....	.001	.13	.0013	2.9	3.1
D.....	.001	.10	.0010	3.8
D¹.....	.002	.10	.0020	3.8	3.9
E.....	.001	.19	.0019	4.7	4.6
F.....	.001	.19	.0019	4.4	4.8

In the above series the physiological activity of thyroid containing 0.11, 0.13 (two samples), 0.10, and 0.19 per cent (two samples) of iodine was compared; the preparations were from different manufacturers and were received at different times. Three of the samples with the lower percentages of iodine produced approximately equal effects. The two samples with the higher percentages also produced equal effects; the latter were nearly twice as great as those produced by the former. Moreover, one of the weaker preparations, in twice the amount, produced an effect about equal to that of one of the stronger ones. We encountered in this series one of the few exceptions to the general rule that the physiological activity of a thyroid preparation is parallel to the iodine content. The preparation D, containing 0.1 per cent iodine, was as active as E and F, which contained 0.19 per cent iodine. Possibly there was some error in the weighing of the thyroid or the making of the cakes. In an earlier series with the same preparations the ones with the larger percentages of iodine were about twice as active as the one with the smaller percentage of iodine.

SERIES VII.

In this series the comparative physiological activity of two samples of a commercial preparation. Thyraden, was determined; the results with a sample of desiccated sheep thyroid containing very nearly the same percentage of iodine are introduced for the sake of comparison.

A. THYRADEN (A); 0.085 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
July 3.....	15.87	Feeding of cakes each containing 0.001 gm. thyraden commenced.
9.....	14.43	
11.....	13.57	
12.....		Acetonitrile, 8.14 mgms., i. e., 0.6 mgm. per gm. mouse. Survived.
July 3.....	16.05	Thyraden as above.
9.....	14.10	
11.....	14.00	
12.....		Acetonitrile, 9.24 mgms., i. e., 0.66 mgm. per gm. mouse. Survived.
July 3.....	14.59	Thyraden as above.
9.....	13.50	
11.....	13.33	
12.....		Acetonitrile, 10 mgms., i. e., 0.75 mgm. per gm. mouse. Died 1½ hours.
July 3.....	13.42	Thyraden as above.
9.....	10.41	
11.....	9.85	Acetonitrile, 9.85 mgms., i. e., 1 mgm. per gm. mouse. Died 1¾ hours.

B. THYRADEN (B); 0.085 PER CENT IODINE.

1908.		
July 3.....	15.38	Feeding of cakes each containing 0.001 gm. thyraden commenced.
9.....	14.28	
11.....	14.44	
12.....		Acetonitrile, 6.50 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
July 3.....	11.37	Thyraden as above.
9.....	10.97	
~ 11.....	10.60	
12.....		Acetonitrile, 5.30 mgms., i. e., 0.5 mgm. per gm. mouse. Survived.
July 3.....	15.00	Thyraden as above.
9.....	13.98	
11.....	12.21	
12.....		Acetonitrile, 6.72 mgms., i. e., 0.55 mgm. per gm. mouse. Died 2½ hours.
July 3.....	15.83	Thyraden as above.
9.....	15.20	
11.....	15.65	Acetonitrile, 10.96 mgms., i. e., 0.7 mgm. per gm. mouse. Died 2½ hours.

C. SHEEP THYROID; 0.092 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
July 3.....	15.90	Feeding of cakes each containing 0.001 gm. thyroid begun.
9.....	14.84	
11.....	15.05	
12.....		Acetonitrile, 6.77 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
July 3.....	14.14	Thyroid as above.
9.....	13.44	
11.....	13.50	
12.....		Acetonitrile, 8.1 mgms., i. e., 0.6 mgm. per gm. mouse. Died 1½ hours.
July 3.....	17.79	Thyroid as above.
9.....	15.75	
11.....	15.80	
12.....		Acetonitrile, 11.85 mgms., i. e., 0.75 mgm. per gm. mouse. Died 2¼ hours.
July 3.....	12.67	Thyroid as above.
9.....	11.82	
11.....	10.90	Acetonitrile, 11.99 mgms., i. e., 1.1 mgms. per gm. mouse. Died 1½ hours.

D. SHEEP THYROID; 0.092 PER CENT IODINE.

1908.		
July 3.....	13.73	Feeding of cakes each containing 0.0005 gm. thyroid commenced.
9.....	12.52	
11.....	12.49	
13.....	11.95	Acetonitrile, 3.94 mgms., i. e., 0.33 mgm. per gm. mouse. Survived.
July 3.....	16.90	Thyroid as above.
9.....	15.74	
11.....	15.44	
12.....		Acetonitrile, 5.87 mgms., i. e., 0.38 mgm. per gm. mouse. Died 2¼ hours.
July 3.....	14.95	Thyroid as above.
9.....	13.23	
11.....	12.92	
12.....		Acetonitrile, 5.81 mgms., i. e., 0.45 mgm. per gm. mouse. Died 2 hours.

E. THYRADEN (A); 0.085 PER CENT IODINE.

1908.		
July 3.....	19.41	Feeding of cakes each containing 0.002 gm. thyraden commenced.
9.....	17.13	
11.....	16.02	Acetonitrile, 19.22 mgms., i. e., 1.2 mgms. per gm. mouse. Survived.
July 3.....	10.77	Thyraden as above.
9.....	8.52	
11.....	8.25	
12.....		Acetonitrile, 10.72 mgms., i. e., 1.3 mgms. per gm. mouse. Died 2 hours.
July 3.....	14.15	Thyraden as above.
9.....	10.66	
11.....	9.40	
12.....		Acetonitrile, 15.24 mgms., i. e., 1.62 mgms. per gm. mouse. Died 2½ hours.

F. THYRADEN (B); 0.085 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
July 3.....	12.98	Feeding of cakes each containing 0.002 gm. thyraden commenced.
9.....	12.42	
11.....	11.78	
12.....		Acetonitrile, 12.96 mgms., i. e., 1.1 mgms. per gm. mouse. Survived.
July 3.....	14.07	Thyraden as above.
9.....	12.72	
11.....	12.77	
12.....		Acetonitrile, 16.6 mgms., i. e., 1.3 mgms. per gm. mouse. Survived.
July 3.....	14.56	Thyraden as above.
9.....	13.80	
11.....	13.27	
12.....		Acetonitrile, 18.57 mgms., i. e., 1.4 mgms. per gm. mouse. Died 2½ hours.
July 3.....	16.24	Thyraden as above.
9.....	13.80	
11.....	13.60	Acetonitrile, 20.40 mgms., i. e., 1.5 mgms. per gm. mouse. Died 3¾ hours.

G. CONTROLS.

1908.		
July 3.....	18.24	Feeding of cakes without thyroid commenced.
9.....	14.45	
10.....		Acetonitrile, 3.03 mgms., i. e., 0.21 mgm. per gm. mouse. Survived.
July 3.....	15.08	Cakes as above.
9.....	13.50	
11.....	13.50	
13.....	12.95	Acetonitrile, 3.5 mgms., i. e., 0.27 mgm. per gm. mouse. Survived.
July 3.....	15.89	Cakes as above.
9.....	13.40	
11.....	13.50	Acetonitrile, 4.05 mgms., i. e., 0.3 mgm. per gm. mouse. Survived.
July 3.....	18.08	Cakes as above.
9.....	17.07	
11.....	17.63	
12.....		Acetonitrile, 5.47 mgms., i. e., 0.31 mgm. per gm. mouse. Died 4½ hours.
July 3.....	16.04	Cakes as above.
9.....	14.12	
11.....	14.86	
12.....		Acetonitrile, 5.05 mgms., i. e., 0.34 mgm. per gm. mouse. Died 3¼ hours.

SUMMARY.

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.001	0.085	0.00085	0.66	0.75
B.....	.001	.085	.00085	.50	.55
C.....	.001	.092	.00092	.45	.6
D.....	.0005	.092	.00046	.33	.38
E.....	.002	.085	.00170	1.2	1.3
F.....	.002	.085	.00170	1.3	1.4
G. Controls.....				.3	.31

These experiments show that the physiological activity of the two samples of Thyraden was approximately the same, in harmony with their equal iodine content. Their activity was not far removed from that of a thyroid preparation containing approximately the same percentage of iodine. Double the amount of Thyraden protected against almost twice the dose of acetonitrile.

SERIES VIII.

The physiological activity of two samples of commercial thyroid tablets were compared in this series. The tablets were pulverized and amounts containing definite quantities of thyroid were fed.

A. THYROID; 0.38 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
September 24...	18.45	Feeding of cakes each containing 0.001 gm. thyroid commenced.
28...	17.42	
October 2	16.95	Acetonitrile, 23.73 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.
September 24...	22.00	Thyroid as above.
28...	22.36	
October 2	20.82	Acetonitrile, 35.39 mgms., i. e., 1.7 mgms. per gm. mouse. Survived.
3		
September 24...	17.28	Thyroid as above.
28...	17.02	
October 2	15.10	Acetonitrile, 27.18 mgms., i. e., 1.8 mgms. per gm. mouse. Survived.
3		
September 24...	14.70	Thyroid as above.
28...	14.66	
October 2	13.20	Acetonitrile, 26.40 mgms., i. e., 2 mgms. per gm. mouse. Died 3 hours.

B. THYROID; 0.38 PER CENT IODINE.

1908.		
September 24...	13.00	Feeding of cakes each containing 0.005 gm. thyroid commenced.
28...	13.54	
October 2	11.75	Acetonitrile, 21.15 mgms., i. e., 1.8 mgms. per gm. mouse. Survived.
September 24...	15.18	Thyroid as above.
28...	15.20	
October 2	11.86	Acetonitrile, 32.20 mgms., i. e., 2.8 mgms. per gm. mouse. Survived.
September 24...	16.40	Thyroid as above.
28...	15.72	
October 2	13.58	Acetonitrile, 47.46 mgms., i. e., 3.5 mgms. per gm. mouse. Survived.
3		
September 24...	15.85	Thyroid as above.
28...	16.12	
October 2	14.49	Acetonitrile, 60.86 mgms., i. e., 4.2 mgms. per gm. mouse. Survived.
3		

C. THYROID; 0.065 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
September 24...	13.35	Feeding of cakes each containing 0.001 gm. thyroid commenced
28...	13.34	
October 2	12.54	Acetonitrile, 5.64 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
September 24...	12.70	Thyroid as above.
28...	12.36	
October 2	11.58	
3		Acetonitrile, 5.79 mgms., i. e., 0.50 mgm. per gm. mouse. Survived.
September 24...	16.10	Thyroid as above.
28...	16.24	
October 2	15.97	
3		Acetonitrile, 9.26 mgms., i. e., 0.58 mgm. per gm. mouse. Died 2½ hours.
September 24...	20.88	Thyroid as above.
28...	20.62	
October 2	17.73	Acetonitrile, 12.41 mgms., i. e., 0.7 mgm. per gm. mouse. Died 1 hour.

D. THYROID; 0.065 PER CENT IODINE.

1908.		
September 24...	19.55	Feeding of cakes each containing 0.005 gm. thyroid commenced.
28...	19.90	
October 2	19.13	Acetonitrile, 22.96 mgms., i. e., 1.2 mgms. per gm. mouse. Survived.
September 24...	13.89	Thyroid as above.
28...	13.70	
October 2	13.60	
3		Acetonitrile, 21.76 mgms., i. e., 1.6 mgms. per gm. mouse. Survived.
September 24...	18.60	Thyroid as above.
28...	18.20	
October 2	17.00	
3		Acetonitrile, 32.3 mgms., i. e., 1.9 mgms. per gm. mouse. Survived.
September 24...	13.15	Thyroid as above.
28...	13.06	
October 2	10.55	Acetonitrile, 21.10 mgms., i. e., 2 mgms. per gm. mouse. Died 2½ hours.

SUMMARY.

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.001	0.38	0.0038	1.8	2.0
B.....	.005	.38	.019	4.2
C.....	.001	.065	.00065	.5	.58
D.....	.005	.065	.00325	1.9	2.00
E. Controls.....					.1

Five times as much thyroid was required in D as in A to produce a given physiological effect; this difference corresponds fairly closely with the differences in the percentages of iodine.

Many other experiments with results similar to the above were performed; a number of them will be reported later in other connections. More than twenty preparations of commercial desiccated thyroids were examined and, with possibly one exception, their

activity was parallel to the iodine content. In the exceptional case the activity seemed to be somewhat less than was anticipated from the percentage of iodine; possibly the thyroid had been overheated in the process of drying or had undergone some decomposition, although there is little evidence that such treatment will materially reduce the activity of thyroid.

Occasionally we encountered a series of experiments in which irregular results were obtained. In such cases the experiments were repeated at least twice and concordant results were obtained. The irregularities had probably resulted from some error in making the cakes or the amount of thyroid fed had been too large or too small to give results which could be compared, or perhaps the mice had not been kept under uniform conditions before the thyroid was fed.

As pointed out elsewhere,^a we have been able to foretell with considerable accuracy the iodine content of a thyroid preparation by comparing its physiological activity with that of another preparation the iodine content of which was known.

iii. EXPERIMENTS WITH THYROID FROM VARIOUS ANIMALS.

One of the present writers^b has shown in a previous publication that there is a parallelism between the amount of iodine and the physiological activity of the thyroid of a number of animals (guinea pig, cat, beef, sheep, hog, etc.). Thus a sample of hog thyroid with 0.33 per cent iodine was about six times as active as one of guinea pig thyroid with 0.05 per cent; a sample of sheep thyroid with 0.176 per cent was approximately three times as active as the guinea pig and but one-half as active as the hog thyroid, etc.

We have been able to extend these observations to the thyroids of a large number of wild animals.^c The results were similar, but the parallelism was not as strict as when thyroids of the same species were compared. The following illustrations may be given: The thyroid of a deer with 0.193 per cent iodine was about three times as active as that of a Barbary sheep with 0.075 per cent; that of the Barbary sheep was more than twice as active as that of a sea lion with 0.022 per cent iodine. The thyroid of a cat with 0.08 per cent iodine was about as active as that of the Barbary sheep with 0.075 per cent, but it was distinctly more active than that of a dog with 0.111 per cent.

If we accept the view that iodine free thyreoglobulin has a low degree of physiological activity, then such slight discrepancies may be explained on the supposition that different thyroids, with equal

^a R. Hunt and A. Seidell, *J. Am. M. Ass.*, Chicago, 1908, **51**, p. 1385.

^b R. Hunt, *J. Am. M. Ass.*, Chicago, 1907, **49**, p. 1324.

^c A few of these results were quoted on pp. 45 and 48.

percentages of iodine, have unequal amounts of this iodine-free material; the latter has a slight but distinct action.

Results similar to the above were obtained with the thyroid both of normal dogs and of dogs which had been fed potassium iodide or iodoform. We also found a parallelism between the iodine content and the physiological activity of a large number of normal and pathological human thyroids. These results will be published in detail in another connection, but the following summaries of a few experiments with human thyroids may be quoted to show how close is the parallelism between iodine content and physiological activity:

SERIES I.—HUMAN THYROID.

No. of specimen.	Gm. thyroid fed daily.	Percentage of iodine.	Mgm. I in thyroid fed.	Fatal dose of acetonitrile in mgm. per gm.	
				Recovered.	Died.
23927.....	0.001	0.05	0.0005	0.18
23821.....	.001	.23	.0023	0.7	.9
23807.....	.001	.26	.0026	.95	1.0
Controls.....13	.14

SERIES II.—HUMAN THYROID.

23927.....	0.001	0.05	0.0005	0.08	0.096
23807.....	.001	.26	.0026	.6	.66
23785.....	.001	.45	.0045	.9	1.00

SERIES III.—HUMAN THYROID.

23927.....	0.001	0.05	0.0005	0.27	0.28
23821.....	.001	.23	.0023	2.0
23785.....	.001	.45	.0045	3.6
Controls.....21	.21

b. EXPERIMENTS ON RATS.

The feeding of thyroid to rats lowers their resistance to acetonitrile; the result is thus just the opposite to that which occurs in the case of mice. This was, however, the result we had expected in all classes of animals. For it seemed probable, if acetonitrile is poisonous only as a result of the liberation of hydrocyanic acid from it in the body, that whatever stimulates metabolism would also hasten the decomposition of the nitrile, with a corresponding greater production of hydrocyanic acid. We do not know whether this is the correct explanation of the effect of thyroid feeding in the case of the rat or not. Some light upon this question could probably be obtained by a study of the excretion in the urine of sulphocyanates. In one experiment of this character no difference was found between the amounts of sulphocyanic acid in the urine of normal and thyroid fed rats after the administration of acetonitrile.^a

^a It may be mentioned in this connection that negative results were obtained in similar experiments upon dogs.

In the present work we were chiefly interested in determining if there is a relation between the percentage of iodine in different thyroid preparations and their effect upon the resistance of rats to acetonitrile. The following experiments show that there is such a relation and that the degree of activity is in general parallel with the iodine content:

SERIES I.

A. THYRADEN; 0.085 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
June 27.....	32	Feeding of cakes each containing 0.001 gm. thyraden commenced.
July 1.....	31	
6.....	30	Acetonitrile, 30 mgms., i. e., 1 mgm. per gm. rat. Survived.
June 27.....	65	Thyraden as above.
July 1.....	68	
6.....	62	Acetonitrile, 86.8 mgms., i. e., 1.4 mgms. per gm. rat. Survived.
June 27.....	48	Thyraden as above.
July 1.....	44	
6.....	45	Acetonitrile, 76.5 mgms., i. e., 1.7 mgms. per gm. rat. Died 5 hours.
7.....		
June 27.....	33	Thyraden as above.
July 1.....	34	
6.....	32	Acetonitrile, 57.6 mgms., i. e., 1.8 mgms. per gm. rat. Survived.
7.....		

B. SHEEP THYROID; 0.11 PER CENT IODINE.

1908.		
June 27.....	29	Feeding of cakes each containing 0.001 gm. thyroid commenced.
July 1.....	29	
6.....	28	Acetonitrile, 25.2 mgms., i. e., 0.9 mgm. per gm. rat. Survived.
7.....		
June 27.....	54	Thyroid as above.
July 1.....	53	
6.....	54	Acetonitrile, 54 mgms., i. e., 1 mgm. per gm. rat. Survived.
June 27.....	31	Thyroid as above.
July 1.....	30	
6.....	29	Acetonitrile, 31.9 mgms., i. e., 1.1 mgms. per gm. rat. Died 3½ hours.
June 27.....	63	Thyroid as above.
July 1.....	61	
6.....	54	Acetonitrile, 70.2 mgms., i. e., 1.3 mgms. per gm. rat. Died about 3 hours.

C. SHEEP THYROID; 0.21 PER CENT IODINE.

1908.		
June 27.....	43	Feeding of cakes each containing 0.001 gm. thyroid commenced.
July 1.....	42	
6.....	42	Acetonitrile, 1.68 mgms., i. e., 0.04 mgm. per gm. rat. Survived.
June 27.....	29	Thyroid as above.
July 1.....	29	
6.....	28	Acetonitrile, 15.40 mgms., i. e., 0.55 mgm. per gm. rat. Survived.
7.....		
June 27.....	40	Thyroid as above.
July 1.....	41	
6.....	39	Acetonitrile, 27.3 mgms., i. e., 0.7 mgm. per gm. rat. Died 1½-2 hours.
June 27.....	61	Thyroid as above.
July 1.....	58	
6.....	54	Acetonitrile, 54 mgms., i. e., 1 mgm. per gm. rat. Died 1¼ hours.

D. SHEEP THYROID; 0.11 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
June 27.....	33	Feeding of cakes each containing 0.0005 gm. thyroid commenced.
July 1.....	32	
6.....	30	Acetonitrile, 45 mgms., i. e., 1.5 mgms. per gm. rat. Survived.
June 27.....	29	Thyroid as above.
July 1.....	30	
6.....	30	
7.....		Acetonitrile, 48 mgms., i. e., 1.6 mgms. per gm. rat. Survived.
June 27.....	46	Thyroid as above.
July 1.....	42	
6.....	45	
7.....		Acetonitrile, 81 mgms., i. e., 1.8 mgms. per gm. rat. Died 4½ hours.
June 27.....	58	Thyroid as above.
July 1.....	57	
6.....	55	Acetonitrile, 104.5 mgms., i. e., 1.9 mgms. per gm. rat. Died 1½ hours.

E. CONTROLS.

1908.		
June 27.....	34	Feeding of cakes without thyroid commenced.
July 1.....	33	
6.....	34	Acetonitrile, 102 mgms., i. e., 3 mgms. per gm. rat. Survived.
June 27.....	30	Feeding of cakes as above.
July 1.....	31	
6.....	30	
7.....		Acetonitrile, 99 mgms., i. e., 3.3 mgms. per gm. rat. Survived.
June 27.....	31	Cakes as above.
July 1.....	29	
6.....	29	
7.....		Acetonitrile, 104.4 mgms., i. e., 3.6 mgms. per gm. rat. Survived.
June 27.....	52	Cakes as above.
July 1.....	49	
6.....	49	
7.....		Acetonitrile, 196 mgms., i. e., 4 mgms. per gm. rat. Died 4 hours.

Summary.—The above results may be tabulated as follows:

	Gm. thy- roid in each cake.	Percentage of iodine in thyroid.	Mgm. I in thyroid in each cake.	Fatal dose of aceto- nitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.001	0.085	0.00085	1.4	1.7
B.....	.001	.11	.0011	1.0	1.1
C.....	.001	.21	.0021	.55	.7
D.....	.0005	.11	.00055	1.6	1.8
E. Controls.....				3.6	4.0

These results show that the thyroids with the higher percentages of iodine were more active in diminishing the resistance of rats to acetonitrile than was that with the lowest percentage. One-half of a milligram of thyroid containing 0.11 per cent iodine was nearly as active as a milligram of thyroid with 0.085 per cent iodine.

SERIES II.

Various amounts of the thyroid of several different animals with different percentages of iodine were fed in this series. The total amount of iodine fed did not vary greatly and the physiological effects were not very different.

A. DOG THYROID; 0.104 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1907.		
July 6.....	124	Feeding of cakes each containing 0.0035 gm. thyroid commenced.
8.....	123	
11.....	120	
15.....	119	
17.....	118	Acetonitrile, 94.4 mgms., i. e., 0.8 mgm. per gm. rat. Survived.
July 6.....	107	Thyroid as above.
8.....	104	
11.....	100	
15.....	98	
17.....	98	Acetonitrile, 98 mgms., i. e., 1 mgm. per gm. rat. Died 3 hours.
July 6.....	73	Thyroid as above.
8.....	70	
11.....	68	
15.....	64	
16.....	63	Acetonitrile, 81.9 mgms., i. e., 1.3 mgms. per gm. rat. Died about 3 hours.
July 6.....	79	Thyroid as above.
8.....	77	
11.....	74	
15.....	68	
16.....	70	Acetonitrile, 126 mgms., i. e., 1.8 mgms. per gm. rat. Died 3½ hours.

B. SHEEP THYROID; 0.176 PER CENT IODINE.

1907.		
July 6.....	122	Feeding of cakes each containing 0.002 gm. thyroid commenced.
8.....	119	
11.....	114	
15.....	105	
16.....	105	Acetonitrile, 94.5 mgms., i. e., 0.9 mgm. per gm. rat. Survived.
July 6.....	106	Thyroid as above.
8.....	106	
11.....	104	
15.....	101	
17.....	102	Acetonitrile, 102 mgms., i. e., 1 mgm. per gm. rat. Survived.
July 6.....	73	Thyroid as above.
8.....	69	
11.....	66	
15.....	62	
17.....	64	Acetonitrile, 76.8 mgms., i. e., 1.2 mgms. per gm. rat. Died 2½ hours.
July 6.....	76	Thyroid as above.
8.....	71	
11.....	70	
15.....	68	
16.....	68	Acetonitrile, 102 mgms., i. e., 1.5 mgms. per gm. rat. Died 4 hours.

C. HOG THYROID; 0.33 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1907.		
July 6.....	142	Feeding of cakes each containing 0.001 gm. thyroid commenced.
8.....	144	
11.....	113	
15.....	106	
17.....	103	
		Acetonitrile, 61.8 mgms., i. e., 0.6 mgm. per gm. rat. Survived.
July 6.....	88	Thyroid as above.
8.....	84	
11.....	81	
15.....	79	
17.....	80	
		Acetonitrile, 64 mgms., i. e., 0.8 mgm. per gm. rat. Died 3 hours.
July 6.....	85	Thyroid as above.
8.....	82	
11.....	79	
15.....	78	
16.....	77	
17.....	78	
		Acetonitrile, 85.8 mgms., i. e., 1.1 mgms. per gm. rat. Died 3 hours.
July 6.....	88	Thyroid as above.
8.....	87	
11.....	85	
15.....	83	
16.....	84	
		Acetonitrile, 109.2 mgms., i. e., 1.3 mgms. per gm. rat. Died about 8 hours

D. CONTROLS.

1907.		
July 6.....	68	Feeding of cakes without thyroid commenced.
8.....	70	
11.....	70	
15.....	67	
16.....	67	
		Acetonitrile, 174 mgms., i. e., 2.6 mgms. per gm. rat. Survived.
July 6.....	103	Cakes as above
8.....	100	
11.....	100	
15.....	97	
16.....	96	
		Acetonitrile, 268.8 mgms., i. e., 2.8 mgms. per gm. rat. Survived.
July 6.....	109	Cakes as above.
8.....	112	
11.....	98	
15.....	85	
17.....	85	
		Acetonitrile, 246.5 mgms., i. e., 2.9 mgms. per gm. rat. Survived.
July 6.....	88	Cakes as above.
8.....	87	
11.....	86	
15.....	85	
		Acetonitrile, 255 mgms., i. e., 3 mgms. per gm. rat. Died 5 hours.
July 6.....	107	Cakes as above.
8.....	91	
11.....	92	
15.....	92	
16.....	90	
17.....	90	
18.....	85	
		Acetonitrile, 275.9 mgms., i. e., 3.1 mgms. per gm. rat. Survived.

SUMMARY.

	Gm. thy- roid in each cake.	Percentage of iodine in thyroid.	Mgm. I in thyroid of each cake.	Fatal dose of ace- tonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.0035	0.104	0.0035	0.8	1.0
B.....	.002	.176	.0035	1.0	1.2
C.....	.001	.33	.0033	.6	.8
D. Controls.....				3.1	3.0

These results show that in order to cause approximately equal physiological effects (as measured by the diminished resistance of the rats to acetonitrile) it was necessary to feed larger amounts of the iodine poor than of the iodine rich thyroid.

SERIES III.

In this series the physiological activity of dog thyroid, the iodine content of which had been increased by the administration of iodoform, was determined. As the results of these experiments are given in detail in Part II (p. 103-5) of this bulletin, only a summary will be given here.

	Gm. thyroid in each cake.	Percentage of iodine.	Mgm. I in thyroid of each cake.	Fatal dose of acetonitrile in mgs. per gm.	
				Recovered.	Died.
A.....	0.0005	0.111	0.00055	1.8	2.1
B.....	.0005	.300	.00150	1.3	1.5
C.....	.0015	.111	.00166	1.2	1.3
D.....	.003	.111	.00333	.9	1.0
E.....	.001	.300	.00300	.5	.6
F. Controls.....				2.9	3.0

GENERAL CONCLUSIONS.

The above series of experiments show that there is a close parallelism between the iodine content of the thyroid and its physiological activity as measured by its effect in diminishing the resistance of rats to acetonitrile.

2. EXPERIMENTS WITH MORPHINE.

It has been shown above that the feeding of thyroid causes an alteration in the resistance of animals to acetonitrile. The effect differs in different species; there is an increased resistance in the case of mice and diminished resistance in rats. In both cases, however, the activity of the thyroid is parallel with its iodine content.

Experiments will now be described in which the effect of feeding thyroid upon the resistance of animals to another poison, morphine,^a was determined. Experiments were made upon mice, rats, and guinea pigs. The resistance of all of these animals to morphine was lowered by the feeding of thyroid and there was a general parallelism between the activity of the different thyroid preparations in this respect and their iodine content.

In performing experiments with morphine it is necessary to observe the precautions noted in the experiments with acetonitrile. Different

^a Similar results were obtained in a few experiments with acetyl-morphine ("heroin") and with codeine.

lots of animals react very differently to morphine; thus in our experiments the fatal dose (by subcutaneous injection) for normal animals has ranged from 0.2 to 0.42 mgm. per gram weight for rats,^a from 0.16 to 0.45 mgm. for mice,^b and from 0.6 to 0.75 mgm. for guinea pigs.^c We were able to find definite relations between the resistance of mice to morphine and the diet which they had received; whether in addition to this effect of diet the age of the animals, their weight or the season, temperature, etc., has an influence we have not been able to definitely determine. Animals which have been kept under uniform conditions react very uniformly to the poison, and it is possible to determine the fatal dose with great accuracy.

These experiments afford another illustration of the folly of determining the "fatal dose" of a poison at the beginning of a long series of experiments, or, as is often done, accepting such a figure as determined by some other investigator and using it as a "control" in a new series of experiments.

a. EXPERIMENTS ON WHITE RATS.

SERIES I.

A. SHEEP THYROID; 0.176 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1907.		
May 30.....	87	Feeding of cakes each containing 0.005 gm. thyroid begun.
June 3.....	81	
7.....	77	
9.....	75	Morphine sulphate, 2.25 mgms., i. e., 0.03 mgm. per gm. rat. Survived.
May 30.....	88	Thyroid as above.
June 3.....	84	
7.....	79	
9.....	77	Morphine sulphate, 3.85 mgms., i. e., 0.05 mgm. per gm. rat. Survived.
May 30.....	107	Thyroid as above.
June 3.....	98	
7.....	94	
9.....	92	Morphine sulphate, 6.44 mgms., i. e., 0.07 mgm. per gm. rat. Survived.

^a T. Sollmann (Textbook of Pharmacology, 2d ed., 1906, p. 954) places the fatal dose of morphine for rats at 0.45 mgm. per gram body weight.

^b J. Morgenroth (Berl. klin. Wchnschr., 1903, 40, p. 471) found the fatal dose of morphine hydrochloride for mice in Frankfort on the Main, to be about 0.93 mgm. per gram.

^c T. Sollmann (l. c.) places the fatal dose of morphine for guinea pigs at 0.7 mgm. per gram.

B. HOG THYROID; 0.33 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1907.		
May 30.....	78	Feeding of cakes each containing 0.005 gm. thyroid begun.
June 3.....	71	
7.....	72	
9.....	67	Morphine sulphate, 1.68 mgms., i. e., 0.025 mgm. per gm. rat. Survived.
May 30.....	77	Thyroid as above.
June 3.....	72	
7.....	70	
9.....	68	Morphine sulphate, 2.72 mgms., i. e., 0.04 mgm. per gm. rat. Died in 3 hours.
May 30.....	101	Thyroid as above.
June 3.....	97	
7.....	89	
9.....	90	Morphine sulphate, 4.5 mgms., i. e., 0.05 mgm. per gm. rat. Died 1½ hours.

C. CONTROLS.

1907.		
May 30.....	93	Feeding of plain cakes begun.
June 3.....	91	
7.....	91	
9.....	91	Morphine sulphate, 27.3 mgms., i. e., 0.3 mgm. per gm. rat. Survived.
May 30.....	79	Cakes as above.
June 3.....	75	
7.....	73	
9.....	74	Morphine sulphate, 25.9 mgms., i. e., 0.35 mgm. per gm. rat. Survived.
May 30.....	92	Cakes as above.
June 3.....	83	
7.....	82	
9.....	80	Morphine sulphate, 32.0 mgms., i. e., 0.4 mgm. per gm. rat. Survived.
June 1.....	46	Cakes as above.
5.....	45	
7.....	45	
11.....	43	Morphine sulphate, 18.06 mgms., i. e., 0.42 mgm. per gm. rat. Died 2 hours.

Summary.—The results of these experiments may be summarized as follows:

	Gm. thyroid in each cake.	Percentage of iodine in thyroid.	Mgm. I in thyroid of each cake.	Average loss of weight in per cent of original weight.	Fatal dose of morphine in mg. per gm.	
					Recovered.	Died.
A.....	0.005	0.176	0.0088	13.4	0.07
B.....	.005	.33	.0165	12.1	.025	0.04
C. Controls.....				7.1	.40	.42

Unfortunately the fatal dose of morphine for rats which had received sheep thyroid, A, was not determined; it was probably twice as great as that for those which had received hog thyroids, B. The sheep thyroid contained about one-half as much iodine as the hog thyroid. Rats receiving the hog thyroid died from one-tenth the amount of morphine necessary to kill the controls. The rats of

all three series lost weight; the controls lost 7.1 per cent. Evidently the exclusive diet of crackers is not suitable for rats. The loss of weight caused by the thyroid was slight if that which would have probably been caused by the crackers alone is deducted, and probably had nothing to do with the increased susceptibility of the animals to morphine.

SERIES II.

A. THYRADEN; 0.085 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
July 14.....	57	Feeding of cakes each containing 0.001 gm. thyraden begun.
18.....	56	
22.....	55	Morphine sulphate, 4.95 mgms., i. e., 0.09 mgm. per gm. rat. Survived.
July 14.....	54	Thyraden as above.
18.....	51	
22.....	49	Morphine sulphate, 5.88 mgms., i. e., 0.12 mgm. per gm. rat. Survived.
July 14.....	52	Thyraden as above.
18.....	48	
22.....	48	Morphine sulphate, 7.20 mgms., i. e., 0.15 mgm. per gm. rat. Died in 5 hours.
July 14.....	50	Thyraden as above.
18.....	48	
22.....	49	
23.....		Morphine sulphate, 12.0 mgms., i. e., 0.16 mgm. per gm. rat. Survived.

B. SHEEP THYROID; 0.12 PER CENT IODINE.

1908.		
July 14.....	60	Feeding of cakes each containing 0.001 gm. thyroid begun.
18.....	55	
22.....	54	Morphine sulphate, 4.32 mgms., i. e., 0.08 mgm. per gm. rat. Survived.
July 14.....	66	Thyroid as above.
18.....	65	
22.....	66	Morphine sulphate, 7.26 mgms., i. e., 0.11 mgm. per gm. rat. Survived.
July 14.....	54	Thyroid as above.
18.....	51	
22.....	53	
23.....		Morphine sulphate, 6.89 mgms., i. e., 0.13 mgm. per gm. rat. Survived.
July 14.....	60	Thyroid as above.
18.....	58	
22.....	59	
23.....		Morphine sulphate, 8.85 mgms., i. e., 0.15 mgm. per gm. rat. Died in 2 hours.

C. SHEEP THYROID; 0.19 PER CENT IODINE.

1908.		
July 14.....	45	Feeding of cakes each containing 0.001 gm. thyroid begun.
18.....	41	
22.....	40	Morphine sulphate, 1.60 mgms., i. e., 0.04 mgm. per gm. rat. Survived.
July 14.....	42	Thyroid as above.
18.....	40	
22.....	38	
23.....		Morphine sulphate, 1.90 mgms., i. e., 0.05 mgm. per gm. rat. Died 4 hours.
July 14.....	44	Thyroid as above.
18.....	43	
22.....	43	Morphine sulphate, 2.58 mgms., i. e., 0.06 mgm. per gm. rat. Died 4 hours.

D. SHEEP THYROID; 0.2 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
July 14.....	33	Feeding of cakes each containing 0.001 gm. thyroid begun.
18.....	31	
22.....	30	Morphine sulphate, 1.50 mgms., i. e., 0.05 mgm. per gm. rat. Survived.
July 14.....	60	Thyroid as above.
18.....	54	
22.....	53	
23.....		Morphine sulphate, 3.18 mgms., i. e., 0.06 mgm. per gm. rat. Died 5 hours.
July 14.....	65	Thyroid as above.
18.....	61	
22.....	62	
23.....		Morphine sulphate, 4.34 mgms., i. e., 0.07 mgm. per gm. rat. Died 2 hours.
July 14.....	40	Thyroid as above.
18.....	40	
22.....	38	Morphine sulphate, 3.04 mgms., i. e., 0.08 mgm. per gm. rat. Died 5½ hours.

E. SHEEP THYROID; 0.19 PER CENT IODINE.

1908.		
July 14.....	61	Feeding of cakes each containing 0.0005 gm. thyroid begun.
18.....	59	
22.....	59	Morphine sulphate, 5.31 mgms., i. e., 0.09 mgm. per gm. rat. Survived.
July 14.....	87	Thyroid as above.
18.....	83	
22.....	81	Morphine sulphate, 8.91 mgms., i. e., 0.11 mgm. per gm. rat. Survived.
July 14.....	52	Thyroid as above.
18.....	49	
22.....	48	Morphine sulphate, 5.76 mgms., i. e., 0.12 mgm. per gm. rat. Died 1½ hours.
July 14.....	75	Thyroid as above.
18.....	71	
22.....	74	
23.....		Morphine sulphate, 9.62 mgms., i. e., 0.13 mgm. per gm. rat. Died 1½ hours.

F. SHEEP THYROID; 0.2 PER CENT IODINE.

1908.		
July 14.....	47	Feeding of cakes each containing 0.0005 gm. thyroid begun.
18.....	46	
22.....	46	Morphine sulphate, 3.68 mgms., i. e., 0.08 mgm. per gm. rat. Survived.
July 14.....	48	Thyroid as above.
18.....	50	
22.....	47	
23.....		Morphine sulphate, 4.23 mgms., i. e., 0.09 mgm. per gm. rat. Survived.
July 14.....	50	Thyroid as above.
18.....	48	
22.....	49	
23.....		Morphine sulphate, 5.29 mgms., i. e., 0.11 mgm. per gm. rat. Died 3½ hours.
July 14.....	47	Thyroid as above.
18.....	45	
22.....	43	Morphine sulphate, 5.16 mgms., i. e., 0.12 mgm. per gm. rat. Died 12 hours.

All of the controls (i. e., rats which had received no thyroid) died, so that we are unable to state the fatal dose. The smallest dose which killed was 0.2 mgm. per gram.

Summary.—The results of these experiments may be summarized as follows:

	Gm. thy- roid in each cake.	Percent- age of iodine in thyroid.	Mgm. I in thyroid in each cake.	Loss of weight in per- cent of original weight.	Fatal dose of mor- phine in mgm. per gm.	
					Recovered.	Died.
A.....	0.001	0.085	0.00085	6.6	0.16	0.15
B.....	.001	.12	.0012	3.3	.13	.15
C.....	.001	.19	.0019	7.6	.04	.05
D.....	.001	.2	.0020	7.6	.05	.06
E.....	.0005	.19	.00095	4.7	.11	.12
F.....	.0005	.2	.001	3.6	.09	.11
G controls.....				1.020

The fatal dose of morphine sulphate for the rats which had received the thyroid with the higher percentages of iodine (0.19 to 0.2) was less than one-half as great as that for those which had received the thyroid with the lower percentages of iodine (0.085 and 0.12). The fatal doses were about the same when but one-half as much of the iodine rich thyroid as of the iodine poor thyroid was fed. There were but slight losses of weight.

SERIES III.

In this series (which was not very complete) the effects of feeding dog thyroid, the iodine content of which had been increased by the administration of iodoform to the dogs, were determined. Since the experiments will be given in detail in Part II (p. 107-9) of this bulletin only the summary is given here.

	Gm. thy- roid in each cake.	Percent- age of iodine in thyroid.	Mgm. I in thyroid in each cake.	Loss of weight in per- cent of original weight.	Fatal dose of mor- phine in mgm. per gm.	
					Recovered.	Died.
A.....	0.0005	0.111	0.00055	7.0	0.25
B.....	.0005	.3	.0015	7.6	.20	0.25
C.....	.0015	.111	.00166	2.425
D.....	.003	.111	.00333	.0	.16	.20
E.....	.001	.106	.00106	5.5	.25
F.....	.001	.3	.00300	14.020
G controls.....				9.1	.39	.40

These experiments show that with equal amounts of thyroid containing different percentages of iodine those with the higher percentages of iodine caused the greater lowering of resistance to morphine; also that in order to obtain equal physiological effects it was necessary to feed much more of the iodine poor than of the iodine rich thyroid. Loss of weight can not explain the increased susceptibility of the rats to morphine, for with but one exception there was no loss of weight greater than that which could be ascribed to the exclusive cracker diet.

SERIES IV.

The following experiments may be quoted for the purpose of illustrating how markedly the resistance of rats to morphine may be reduced by the feeding of thyroid rather than because they bring out the effects of different iodine percentages. The amounts of thyroid fed were selected so as to make the total amount of iodine approximately equal in all cases. Unfortunately the experiments were not sufficiently numerous for us to determine the minimum lethal doses in all cases.

A. DOG THYROIDS; 0.111 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1907.		
June 25.....	189	Feeding of cakes each containing 0.003 gm. thyroid begun.
29.....	181	
July 3.....	181	Morphine sulphate, 7.28 mgms., i. e., 0.04 mgm. per gm. rat. Died 13 hours.
5.....	182	
June 25.....	192	Thyroid as above.
29.....	186	
July 3.....	183	Morphine sulphate, 9.68 mgms., i. e., 0.055 mgm. per gm. rat. Died 4 hours.
6.....	176	
June 25.....	152	Thyroid as above.
29.....	142	
July 3.....	138	Morphine sulphate, 9.66 mgms., i. e., 0.07 mgm. per gm. rat. Died 9 hours.
5.....	138	

B. THYROID OF GUINEA PIG; 0.05 PER CENT IODINE.

1907.		
June 25.....	116	Feeding of cakes each containing 0.007 gm. thyroid begun.
29.....	117	
July 3.....	118	Morphine sulphate, 10.62 mgms., i. e., 0.09 mgm. per gm. rat. Survived.
5.....	118	
June 25.....	156	Thyroid as above.
29.....	155	
July 3.....	155	Morphine sulphate, 15.63 mgms., i. e., 0.1 mgm. per gm. rat. Died 3½ hours.
5.....	156	
June 25.....	106	Thyroid as above.
29.....	101	
July 3.....	100	Morphine sulphate, 12.12 mgms., i. e., 0.12 mgm. per gm. rat. Died 4½ hours.
5.....	101	

C. HOG THYROID; 0.33 PER CENT IODINE.

1907.		
June 25.....	141	Feeding of cakes each containing 0.001 gm. thyroid begun.
29.....	134	
July 3.....	133	Morphine sulphate, 3.99 mgms., i. e., 0.03 mgm. per gm. rat. Died 2¼ hours.
5.....	133	
June 25.....	138	Thyroid as above.
29.....	134	
July 3.....	135	Morphine sulphate, 5.28 mgms., i. e., 0.04 mgm. per gm. rat. Died 2¾ hours.
5.....	132	
June 25.....	155	Thyroid as above.
29.....	149	
July 3.....	146	Morphine sulphate, 8.7 mgms., i. e., 0.06 mgm. per gm. rat. Died 2 hours.
5.....	145	

D. SHEEP THYROID; 0.176 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1907.		
June 25.....	114	Feeding of cakes each containing 0.002 gm. thyroid begun.
29.....	110	
July 3.....	111	
5.....	108	Morphine sulphate, 3.24 mgms., i. e., 0.03 mgm. per gm. rat. Died 20 hours.
June 25.....	158	Thyroid as above.
29.....	150	
July 3.....	150	
6.....	150	Morphine sulphate, 6.75 mgms., i. e., 0.045 mgm. per gm. rat. Died 2 hours.
June 25.....	127	Thyroid as above.
29.....	120	
July 3.....	121	
5.....	120	Morphine sulphate, 7.2 mgms., i. e., 0.06 mgm. per gm. rat. Died 5½ hours.

E. CONTROLS.

1907.		
June 25.....	121	Feeding of plain cakes begun.
29.....	109	
July 3.....	109	
4.....	111	Morphine sulphate, 27.75 mgms., i. e., 0.25 mgm. per gm. rat. Survived.
June 25.....	100	Cakes as above.
29.....	97	
July 3.....	96	
4.....	96	Morphine sulphate, 28.8 mgms., i. e., 0.30 mgm. per gm. rat. Survived.
June 25.....	119	Cakes as above.
29.....	120	
July 3.....	119	
6.....	119	Morphine sulphate, 36.89 mgms., i. e., 0.31 mgm. per gm. rat. Died 5½ hours.
June 25.....	73	Cakes as above.
29.....	71	
July 3.....	72	
5.....	70	Morphine sulphate, 22.4 mgms., i. e., 0.32 mgm. per gm. rat. Died 8 hours.
June 25.....	81	Cakes as above.
29.....	78	
July 3.....	74	
5.....	79	Morphine sulphate, 27.65 mgms., i. e., 0.35 mgm. per gm. rat. Died 2½ hours.

Summary.—The results of the above experiments are shown in the following table:

	Gm. thyroid in each cake.	Percentage of iodine in thyroid.	Mgm. I in thyroid in each cake.	Loss of weight in per cent of original weight.	Fatal dose of morphine in mgm. per gm.	
					Recovered.	Died.
A.....	0.003	0.111	0.0033	7.0	0.04
B.....	.007	.05	.0035	.8	0.09	.10
C.....	.001	.33	.0033	5.503
D.....	.002	.176	.00352	5.203
E. Controls.....	4.0	.30	.31

Although the amounts of thyroid fed varied widely (from 0.001 gm. to 0.007 gm.), there was approximately the same amount of iodine in all cases and, with one exception, the lowering of the resistance seemed to be about equal. In all cases except one fully ten times as much morphine was required to kill the controls as to kill those which had received thyroid. The thyroid caused practically no loss of weight; the very slight loss which occurred can be attributed to the cracker diet.

SUMMARY OF EXPERIMENTS ON RATS.

The above experiments show very clearly that the resistance of rats to morphine is lowered by the feeding of thyroid. In two series the fatal dose for the thyroid-fed rats was but one-tenth that for the controls. They also show that the activity of different thyroid preparations in this respect is closely parallel to their iodine content. It would doubtlessly be possible to determine with a fair degree of accuracy the percentage of iodine in a thyroid preparation by comparing its physiological activity with that of another preparation containing a known percentage of iodine. The increased susceptibility to morphine is entirely independent of any loss of weight; it can evidently not be attributed to a "general lowering of resistance" such as may be supposed to occur when there is a loss of weight from starvation.^a

b.—EXPERIMENTS ON MICE.

The results of the experiments on mice were somewhat irregular. There was invariably, however, an increased susceptibility to morphine as a result of the feeding of thyroid. As a rule the thyroid containing the larger percentage of iodine had the greater effect but there were many exceptions which we are unable to explain. It would probably be impossible to detect small variations in the percentage of iodine in different thyroid preparations from their effects upon the resistance of mice to morphine.

As these experiments do not offer many points of special interest they will be reproduced in abstract only. The average loss of weight, expressed in percentage of original weight, is given in the last column.

^aStarvation markedly increases the resistance of animals to some poisons; this is the case, for example, with acetonitrile. (See R. Hunt, *Studies in Experimental Alcoholism*, Bull. 33, Hygienic Laboratory, 1907, p. 34.)

SERIES I.—SHEEP THYROID.

	Gm. thy- roid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of morphine in mgm. per gm.		Loss in weight in percentage of original weight.
				Recovered.	Died.	
A.....	0.001	0.085	0.00085	0.17	0.25	9.0
B.....	.001	.11	.0011	.09	.11	14.3
C.....	.001	.11	.0011	.12	.16	5.7
D.....	.001	.19	.0019	.12	.14	10.7
E.....	.001	.21	.0021	.13	.16	14.6
F. Controls.....				.19	.20	9.9

The resistance of mice to morphine was uniformly diminished by the thyroid. The thyroid having the least effect was the preparation containing the smallest percentage of iodine; the effects of the other preparations were nearly equal, although some contained nearly twice as much iodine as others. There was no constant relation between the loss of weight and the diminished resistance to morphine.

SERIES II.

	Gm. thy- roid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose in mgm. per gm.		Loss in weight.
				Recovered.	Died.	
A.....	0.005	0.085	0.00425	0.17	0.18	8.9
B.....	.005	.11	.0055	.08	.11	13.2
C.....	.005	.19	.0095	.09	.10	8.5
D.....	.005	.21	.0105	.07	.09	28.5
E.....	.01	.1	.01	.10	.12	15.1
F.....	.01	.11	.011	.18	.14	16.5
G.....	.01	.11	.011	.105	.12	13.6
H.....	.01	.11	.011	.13	.16	14.2
I.....	.01	.19	.019	.08	.09	15.0
J.....	.01	.21	.021	.06	.08	9.4
K. Controls.....				.17	.18	7.5

The thyroid with the largest percentage of iodine was the most active when the smaller (0.005 gm.) as well as when the larger (0.01 gm.) amounts of thyroid were fed. In some cases the loss of weight was parallel with the increased susceptibility to morphine; in other cases it was not.

SERIES III.

	Gm. thy- roid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose in mgm. per gm.		Loss in weight. ^a
				Recovered.	Died.	
A.....	0.01	0.05	0.005	0.18	0.22	- 3.0
B.....	.01	.104	.0104	.11	.16	5.8
C.....	.01	.19	.019009	18.0
D.....	.01	.298	.0298	.09	.10	11.7
E.....	.01	.33	.0330	.07	.09	2.4
F. Controls.....				.48	.45	- 3.7

^a The + sign indicates that the mice had increased in weight.

With the increased percentage of iodine in the thyroid there was, with one exception, a uniform increase in physiological activity, as shown by the increased susceptibility to morphine.

The changes in weight were in most cases not marked; in two instances there was a slight increase. The most marked change was with the mice of group C; the average loss of weight with these was 18 per cent. Perhaps this indicates that the mice of this series had eaten more of the cakes than had the mice of the other series.

The following series may be quoted as additional illustrations of how the susceptibility of mice to morphine may be increased by the administration of thyroid:

SERIES IV.

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mg. I in thyroid fed daily.	Fatal dose in mgm. per gm.		Loss in weight. ^a
				Recovered.	Died.	
A.....	0.01	0.19	0.019	0.10	0.15	5.1
B. Controls.....				.36		+6.8

SERIES V.

A.....	0.03	0.186	0.0558	0.18	0.22	14.2
B. Controls.....				.38	.43	7.9

SERIES VI.^a

A.....	0.2	0.186	0.0372	0.07	0.08	1.9
B. Controls.....				.24	.24	1.5

^a The + sign indicates that the mice had increased in weight.

^b The experiment was continued but six days instead of ten, as was usually the case.

SUMMARY OF EXPERIMENTS ON MICE.

The above experiments show that the resistance of mice to morphine was uniformly lowered by the feeding of thyroid. This lowering of the resistance occurred independently of the changes in weight; in some cases there was a markedly increased susceptibility to morphine with an increase in weight. In general the thyroid containing the higher percentages of iodine caused the greatest changes in resistance, but there were a number of exceptions.

c.—EXPERIMENTS ON GUINEA PIGS.

Experiments were not made in which the effects of thyroid containing different percentages of iodine upon the resistance of guinea pigs to morphine were determined. The following experiments show that the resistance of these animals to morphine is diminished by the feeding of thyroid. The amount of thyroid was very large; in the

second series there was a loss of weight, while in the first there was only a retardation of growth:

SERIES I.

A. SHEEP THYROID; 0.084 PER CENT IODINE.

Date.	Weight of pig.	Remarks.
1907.		
May 1.....	265	Feeding of thyroid, 0.120 gm. daily, begun.
4.....	265	
8.....	260	
10.....	260	
13.....	275	Morphine sulphate, 55 mgms., i. e., 0.2 mgm. per gm. pig. Survived.
May 1.....	330	Thyroid as above.
4.....	330	
8.....	320	
11.....	315	
15.....	267	Morphine sulphate, 66.75 mgms., i. e., 0.25 mgm. per gm. pig. Died 16 hours.
May 1.....	285	Thyroid as above.
4.....	280	
8.....	280	
11.....	280	
14.....	259	Morphine sulphate, 77.7 mgms., i. e., 0.3 mgm. per gm. pig. Died 8½ hours.
May 1.....	215	Thyroid as above.
4.....	200	
8.....	215	
11.....	215	
14.....	208	Morphine sulphate, 83.2 mgms., i. e., 0.4 mgm. per gm. pig. Died 3 hours.

B. CONTROLS.

1907.		
May 1.....	320	
4.....	335	
9.....	360	
13.....	385	
14.....	348	Morphine sulphate, 174 mgms., i. e., 0.5 mgm. per gm. pig. Survived.
May 1.....	200	
4.....	210	
9.....	220	
13.....	275	
15.....	250	Morphine sulphate, 150 mgms., i. e., 0.6 mgm. per gm. pig. Died 3 hours.
May 1.....	225	
4.....	240	
9.....	275	
13.....	305	Morphine sulphate, 213.5 mgms., i. e., 0.7 mgm. per gm. pig. Died 3¼ hours.

SERIES II.

A. SHEEP THYROID; 0.084 PER CENT IODINE.

Date.	Weight of pig.	Remarks.
1907.		
April 4.....	265	Feeding of thyroid, 0.24 gm. daily, begun.
8.....	232	
12.....	220	
16.....	195	Morphine sulphate, 48.75 mgms., i. e., 0.25 mgm. Died 10 to 15 hours.
April 4.....	244	Thyroid as above.
8.....	235	
12.....	255	
14.....	256	Morphine sulphate, 76.8 mgms., i. e., 0.3 mgm. per gm. pig. Died 21 hours.
April 4.....	260	Thyroid as above.
8.....	225	
12.....	215	
14.....	217	Morphine sulphate, 108.5 mgms., i. e., 0.5 mgm. per gm. pig. Died 4 hours.

B. CONTROLS.

1907.		
April 4.....	250	
8.....	270	
12.....	300	
14.....	302	Morphine sulphate, 196.3 mgms., i. e., 0.65 mgm. per gm. pig. Survived.
April 4.....	252	
8.....	280	
12.....	315	
15.....	335	Morphine sulphate, 251.25 mgms., i. e., 0.75 mgm. per gm. pig. Died 3½ hours.
April 4.....	240	
8.....	275	
12.....	290	
14.....	307	Morphine sulphate, 245.6 mgms., i. e., 0.8 mgm. Died 2 hours.

Summary. The results of the above experiments may be summarized as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose in mgm. per gm.		Average loss of weight in per cent of original weight. ^a
				Recovered.	Died.	
Series I.....	0.12	0.084	0.1008	0.2	0.25	7.9
Controls.....				.5	.60	+21.2
Series II.....	.24	.084	.2016		.25	13.1
Controls.....				.65	.75	+27.2

^a The + sign indicates that the guinea-pigs had increased in weight.

The guinea pigs which had received the thyroid died from one-third to one-half of the dose of morphine fatal to the controls. The amount of thyroid fed was very large and the animals were evidently deeply intoxicated.

Conclusions from the experiments with morphine.

The resistance of rats, mice, and guinea pigs to morphine is uniformly lowered by the feeding of thyroid. This occurs independently of any effect the thyroid may have upon the weight of the animals. In the case of the rat there is a close parallelism between the physiological effect of the thyroid, as determined by the increased susceptibility to morphine, and the percentage of iodine. A similar parallelism was found, in general, in the experiments on mice; the animals which had received thyroid with a higher percentage of iodine almost invariably died from a smaller dose of morphine than did those which had received thyroid with a low percentage of iodine. The question of the relation between the iodine content and the physiological activity of the thyroid was not tested on guinea pigs. The results of the experiments with morphine on rats and mice are therefore an additional argument for the view that the degree of physiological activity of thyroid is parallel to the iodine content.

We have no explanation to offer for the effect of thyroid feeding upon the resistance of animals to morphine further than the suggestion made by one of us in a previous paper:^a

I have not been able to determine the cause of this increased susceptibility; possibly the thyroid, which is known to hasten the oxidation of fats, affects the lipoids of the nervous system in such a manner that poisons, such as morphine, gain access to it more easily.

Mansfeld^b found that rabbits which had been deprived of food for a few days were much more susceptible to morphine than were normal rabbits; he endeavored to explain this in the terms of the Meyer-Overton theory of narcosis: In starvation there is a diminution of fat in the body, except in the central nervous system; as a result of this a larger proportion of the fat soluble narcotic is taken up by the nervous system, and so is able to exert a greater toxic action. Although thyroid has a tendency to cause a diminution of fat in the body, we do not believe that this can have played a large part in our experiments; in some of these the thyroid had increased the susceptibility of the animals to morphine ten times without causing any change in weight.

These experiments may have some bearing upon the use of morphine in exophthalmic goiter (hyperthyroidism). There seems to be unanimity of opinion among clinicians that general anæsthetics are very dangerous in this condition:^c The opinions differ as to the use

^a R. Hunt, J. Am. M. Ass., Chicago, 1907, **49**, p. 1325.

^b G. Mansfeld, Arch. internat. de pharmacodynamie et de thérapie, 1905, **15**, p. 467.

^c cf. Th. Kocher, Verhandl. d. deutsch. Gesellsch. f. Chir., Berl., 1901, 30te Kong., p. 346; A. Kocher, Mitt. a. d. Grenzgeb. d. Med. u. Chir., Jena, 1902, **9**, p. 1. Angerer (Münch. m. Wechschr., 1896, **43**, p. 71) states that the feeding of thyroid to patients with goiter renders them especially liable to heart failure when a general anæsthetic is administered.

of morphine or opium. Thus Tyson^a considers opium to be a rational remedy, although he states that Ord and MacKenzie found that it is not well borne; Tyson prefers codeine. Our experiments showed that morphine is very toxic to animals in which a condition of thyroidism has been produced. Of course it has not been conclusively proved that there is a condition of hyperthyroidism in exophthalmic goiter or that man would react to morphine in the same way as do the lower animals. If we may judge of the degree of thyroidism from the loss of weight, our animals were as a rule certainly less deeply intoxicated than are many patients with exophthalmic goiter.

The increased susceptibility to morphine of animals to which thyroid has been fed is suggestive in another connection.

May not many of the very diverse symptoms which occur in exophthalmic goiter be secondary, i. e., may not the condition of hyperthyroidism render many of the organs abnormally sensitive to poisons originating in the body itself (possibly products of intestinal putrefaction) or introduced from without (substances contained in meat, for example)? Organs rendered hypersensitive by the thyroid secretion may respond to amounts of such poisons ordinarily too small to produce any symptoms, just as the thyroid-fed rats may die from doses of morphine which would ordinarily be entirely innocuous.

As is well known there are few diseases in which so many drugs and forms of treatment have been recommended, often apparently with good reason, as in the case of exophthalmic goiter. Perhaps the effect of these is entirely secondary, i. e., some intestinal antiseptics^b may check the formation of injurious substances, others may diminish the irritability of an over-stimulated organ.

^a J. Tyson, *Internat. Clin., Phila.*, 1906, Series 16, **1**, p. 3.

^b *cf.* W. H. Thomson, *Am. J. Med. Sci.*, 1908, **135**, p. 313.

Part II.

ON THE NATURE OF THE RELATION BETWEEN THE IODINE PERCENTAGE AND THE PHYSIOLOGICAL ACTIVITY OF THYROID.

It has been shown above that there is almost invariably a parallelism between the iodine content of thyroid and its physiological activity. The nature of this relation may now be discussed. Some of the writers who recognize that there is such a parallelism hold that the larger amount of iodine in the more active thyroid is a result and not the cause of the greater activity. In other words, according to this view, the more active the gland the larger the amount of iodine with which its substance can combine.^a

The arguments advanced for this theory are in part the same as those which have been urged against the view that the iodine is an important constituent of the thyroid and which have been discussed above. Such arguments are based largely upon what may be called statistical studies, and, as we have already seen, conclusions drawn from such studies do not necessarily apply to the thyroid when used as a drug. Moreover, were this view correct, we should expect to find at times thyroid poor in iodine but with a high degree of physiological activity, for the amount of iodine present in the thyroid is to a considerable extent accidental, being dependent upon the amount of this element available in the food. We have, however, never found a specimen of thyroid with a low percentage of iodine and with a high degree of physiological activity. Whether from the same or from widely separated species, the activity was in general parallel with the iodine content.

A stronger argument against the view that the activity of thyroid is independent of the percentage of iodine is found in a metabolism experiment of Roos,^b in which the activity of normal thyroid was compared with that of thyroid which had combined with a larger amount of iodine *in vivo*. Roos found the iodine-free thyroid of a dog to be without appreciable effect upon nitrogen excretion, whereas an equal amount of thyroid from a dog which had received 20 grams of potassium iodide in eighteen days and which contained 0.35 per cent iodine had a very distinct effect. Only one experiment was performed, and the result, although distinct, was not very marked.^c

^a cf. S. J. Meltzer, N. Yorker med. Monatschr., 1907, **19**, p. 223.

^b E. Roos, Ztschr. f. physiol. Chem., Strassb., 1899, **28**, p. 47.

^c cf. F. Blum, Verhandl. d. Kong. f. inn. Med., 1906, **23**, p. 196.

Moreover, the evidence is far from conclusive that there may not have been differences between the two thyroid preparations other than that of the iodine content. There is also the possibility to be considered that the potassium iodide that was administered during the course of eighteen days had in some way simply stimulated the thyroid to an increased production of an active substance and that this active substance secondarily retained an additional amount of iodine and that the increased activity of the gland was due to the former and not to the latter.

It seemed to us that the following conditions should be fulfilled in order to make an experiment of this character conclusive: There should be evidence that the thyroid of the animals which received the iodine compound was, before its administration, in approximately the same condition as those which were to serve as controls; and, in the second place, the iodine should be administered for but a short time, so as to exclude any prolonged stimulating action. We endeavored to meet these conditions as follows: The thyroids of several groups of ten dogs each were analyzed for iodine, so as to obtain data as to the usual percentage of iodine present. To similar groups of ten dogs two doses of potassium iodide or of iodoform were given on successive days and the dogs killed on the third or fourth day. It was found that a large amount of iodine was taken up by the thyroid and that the latter, tested by our methods, showed greatly increased activity. Moreover, the increased activity was in direct proportion to the amount of iodine which had been taken up by the thyroid. We believe the conclusion is justified that the physiological activity of the thyroid from the different groups of dogs was approximately the same before the iodine was given, and therefore the increased activity of the thyroid of the iodine-fed dogs must have been due entirely to the iodine absorbed. The increased activity appeared much too rapidly to permit of the supposition that the iodine had simply accelerated the production of a more powerful substance independent of the iodine. The experiments were as follows:

SERIES A.

Forty-six dogs were divided into five groups. There were ten animals in each of the first three groups, seven in the fourth, and nine in the fifth. To each of the dogs of the fourth group from 1.5 to 2 grams of potassium iodide were given *per os*; they were killed twenty-four hours later. Each of the dogs of the fifth group received 1 to 1.3 grams iodoform in capsules; this was repeated on the following day and the dogs killed on the third day. The thyroids from all these dogs were weighed, ground up finely, dried at 50° C. and again weighed, and the iodine determined.

Group.	Weight of thyroid fresh.	Weight of thyroid dried.	Per cent of water.	Per cent of iodine.
1.....	18.03	4.84	73.15	0.129
2.....	25.67	6.86	73.27	.111
3.....	14.09	3.99	71.68	.106
4 (fed KI).....	13.25	3.35	74.71	.148
5 (fed CHI_3).....	25.92	7.22	72.14	.30

The glands of the controls contained from 0.106 to 0.129 per cent iodine; those which had received the potassium iodide had 0.148 and those which had received the iodoform 0.3 per cent. The glands of all five series lost approximately the same per cent of moisture on drying; this is additional evidence that they are strictly comparable.

The following experiments were performed with these preparations:

I. EXPERIMENTS WITH ACETONITRILE.

a. EXPERIMENTS ON MICE.

SERIES I.

A. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
June 5.....	12.05	Feeding of cakes each containing 0.0025 gms. thyroid commenced.
8.....	12.92	
11.....	12.92	
15.....	13.07	
16.....	12.63	Acetonitrile, 15.16 mgms., i. e., 1.2 mgms. per gm. mouse. Survived.
June 5.....	10.73	Thyroid as above.
8.....	11.07	
11.....	10.85	
15.....	10.50	
16.....	10.75	Acetonitrile, 15.05 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.
June 5.....	12.95	Thyroid as above.
8.....	13.42	
11.....	11.77	
15.....	10.41	
		Acetonitrile, 16.66 mgms., i. e., 1.6 mgms. per gm. mouse. Died 3 hours.
June 5.....	14.22	Thyroid as above.
8.....	13.82	
11.....	13.00	
15.....	11.60	
		Acetonitrile, 23.2 mgms., i. e., 2 mgms. per gm. mouse. Died 1 hour.

B. THYROID OF GROUP 4 (POTASSIUM IODIDE); 0.148 PER CENT IODINE.

1907.		
June 5.....	11.06	Feeding of cakes each containing 0.0025 gm. thyroid commenced.
8.....	12.27	
11.....	12.35	
15.....	12.00	
		Acetonitrile, 19.2 mgms., i. e., 1.6 mgms. per gm. mouse. Survived.
June 5.....	11.64	Thyroid as above.
8.....	11.52	
11.....	11.52	
15.....	12.15	
16.....	11.80	Acetonitrile, 22.42 mgms., i. e., 1.9 mgms. per gm. mouse. Died 1½ hours.
June 5.....	12.74	Thyroid as above.
8.....	12.02	
11.....	11.62	
15.....	11.11	
16.....	10.94	Acetonitrile, 24.07 mgms., i. e., 2.2 mgms. per gm. mouse. Died 3¼ hours.

C. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
June 5.....	12.52	Feeding of cakes each containing 0.0025 gm. thyroid commenced.
8.....	13.70	
11.....	13.20	
14.....	12.89	Acetonitrile, 18.05 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.
June 5.....	14.01	Thyroid as above.
8.....	14.90	
11.....	13.70	
15.....	12.30	Acetonitrile, 22.14 mgms., i. e., 1.8 mgms. per gm. mouse. Survived.
June 5.....	13.30	Thyroid as above.
8.....	13.13	
11.....	13.20	
15.....	12.18	
16.....	12.10	Acetonitrile, 30.25 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
June 5.....	11.79	Thyroid as above.
8.....	11.83	
11.....	11.40	
15.....	10.18	
16.....	9.23	
17.....	8.71	Acetonitrile, 24.39 mgms., i. e., 2.8 mgms. per gm. mouse. Died 2 hours.

D. CONTROLS.

1907.		
June 5.....	12.48	Feeding of cakes without thyroid commenced.
8.....	13.61	
11.....	13.42	
15.....	12.96	Acetonitrile, 4.28 mgms., i. e., 0.33 mgm. per gm. mouse. Survived.
June 5.....	8.23	Cakes as above.
8.....	7.56	
11.....	8.07	
14.....	8.05	Acetonitrile, 2.98 mgms., i. e., 0.37 mgm. per gm. mouse. Survived.
June 5.....	12.10	Cakes as above.
8.....	13.16	
11.....	12.97	
14.....	13.00	Acetonitrile, 5.2 mgms., i. e., 0.4 mgm. per gm. mouse. Died about 2 hours.
June 5.....	12.30	Cakes as above.
8.....	11.83	
11.....	12.57	
15.....	12.66	
16.....	12.22	Acetonitrile, 4.89 mgms., i. e., 0.4 mgm. per gm. mouse. Died 2 hours.

Summary.—The results of the above experiments may be tabulated as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.0025	0.111	0.0027	1.4	1.6
B.....	.0025	.148	.0037	1.6	1.9
C.....	.0025	.300	.0075	2.5	2.8
D. Controls.....				.37	.40

From the above experiments it is seen that there is a direct parallelism between the per cent of iodine and the physiological activity of the thyroid. The thyroid of Group 5 (C) (from the dogs which had received iodoform and which contained 0.3 per cent iodine) enabled the mice to recover from about twice as much acetonitrile as did that from Group 2 (A) (normal, 0.111 per cent iodine). The thyroid of Group 4 (B) (potassium iodide fed dogs; 0.148 per cent iodine) was slightly more active than that of Group 2 and less active than that of Group 5. The amount of thyroid fed was comparatively large, and in the case of Group 5 was probably greater than the minimum amount necessary to produce the maximum effect.

SERIES II.

In the following experiments different amounts of the thyroid were fed; in the first three the amounts were selected so as to make the total iodine about the same in all.

A. THYROID OF GROUP 3 (NORMAL); 0.106 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
April 14.....	15.30	Feeding of cakes each containing 0.003 gm. thyroid commenced.
17.....	16.02	
20.....	16.37	
22.....	15.99	Acetonitrile, 34.38 mgms., i. e., 2.15 mgms. per gm. mouse. Survived.
April 14.....	21.60	Thyroid as above.
17.....	21.64	
20.....	21.34	
22.....	22.10	
23.....	22.03	Acetonitrile, 55.08 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
April 14.....	23.58	Thyroid as above.
17.....	24.74	
20.....	24.64	
23.....	25.05	Acetonitrile, 67.64 mgms., i. e., 2.7 mgms. per gm. mouse. Died one-half hour.
April 14.....	27.56	Thyroid as above.
17.....	27.72	
20.....	27.50	
23.....	28.30	Acetonitrile, 89.9 mgms., i. e., 3 mgms. per gm. mouse. Died 2 hours.

B. THYROID OF GROUP 4 (POTASSIUM IODIDE); 0.148 PER CENT IODINE.

1908.		
April 14.....	24.70	Feeding of cakes each containing 0.002 gm. thyroid commenced.
17.....	23.62	
20.....	23.57	
22.....	22.70	Acetonitrile, 56.75 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
April 14.....	19.12	Thyroid as above.
17.....	19.58	
20.....	19.68	
23.....	19.52	Acetonitrile, 50.75 mgms., i. e., 2.6 mgms. per gm. mouse. Survived.
April 14.....	15.10	Thyroid as above.
17.....	16.14	
20.....	16.14	
23.....	15.82	Acetonitrile, 45.88 mgms., i. e., 2.9 mgms. per gm. mouse. Survived.
April 14.....	22.72	Thyroid as above.
17.....	24.32	
20.....	24.92	
22.....	25.32	
23.....	25.50	Acetonitrile, 73.95 mgms., i. e., 2.9 mgms. per gm. mouse. Died 1½ hours.

C. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
April 14.....	22.95	Feeding of cakes each containing 0.001 gm. thyroid commenced.
17.....	22.64	
20.....	22.20	
22.....	23.02	Acetonitrile, 46.04 mgms., i. e., 2 mgms. per gm. mouse. Survived.
April 14.....	13.76	Thyroid as above.
17.....	14.03	
20.....	12.58	
23.....	12.50	Acetonitrile, 37.5 mgms., i. e., 3 mgms. per gm. mouse. Survived.
April 14.....	16.66	Thyroid as above.
17.....	17.24	
20.....	17.49	
23.....	17.70	Acetonitrile, 51.33 mgms., i. e., 2.9 mgms. per gm. mouse. Died 2½ hours.
April 14.....	24.36	Thyroid as above.
17.....	23.27	
20.....	23.52	
22.....	24.03	
23.....	23.36	Acetonitrile, 74.75 mgms., i. e., 3.2 mgms. per gm. mouse. Died one-half hour.

D. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

1908.		
April 14.....	19.36	Feeding of cakes each containing 0.002 gm. thyroid commenced.
17.....	19.70	
20.....	20.26	
22.....	20.74	Acetonitrile, 67.4 mgms., i. e., 3.25 mgms. per gm. mouse. Survived.
April 14.....	17.75	Thyroid as above.
17.....	18.85	
20.....	18.57	
22.....	18.42	
23.....	18.44	Acetonitrile, 73.76 mgms., i. e., 4 mgms. per gm. mouse. Survived.
April 14.....	14.94	Thyroid as above.
17.....	15.36	
20.....	15.28	
23.....	15.33	Acetonitrile, 67.45 mgms., i. e., 4.4 mgms. per gm. mouse. Survived.
April 14.....	24.09	Thyroid as above.
17.....	26.07	
20.....	25.45	
23.....	25.33	
24.....	25.15	Acetonitrile, 125.75 mgms., i. e., 5 mgms. per gm. mouse. Died 2 hours.

E. CONTROLS.

1908.		
April 14.....	17.56	Feeding of cakes without thyroid commenced.
17.....	17.76	
20.....	16.42	
23.....	16.71	Acetonitrile, 10.86 mgms., i. e., 0.65 mgm. per gm. mouse. Survived.
April 14.....	27.94	Cakes as above.
17.....	28.76	
20.....	28.58	
23.....	27.83	Acetonitrile, 19.94 mgms., i. e., 0.72 mgm. per gm. mouse. Survived.
April 14.....	19.90	Cakes as above.
17.....	19.62	
20.....	19.34	
22.....	19.90	
23.....	19.44	Acetonitrile, 14.58 mgms., i. e., 0.75 mgm. per gm. mouse. Died 2 hours.
April 14.....	23.54	Cakes as above.
17.....	23.86	
20.....	23.92	
23.....	23.54	
24.....	23.04	Acetonitrile, 17.74 mgms., i. e., 0.77 mgm. per gm. mouse. Died 1½ hours.

Summary.—The results of the foregoing experiments may be tabulated as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.003	0.106	0.00318	2.5	2.7
B.....	.002	.148	.00296	2.9	2.9
C.....	.001	.300	.0030	3.0	2.9
D.....	.002	.300	.0060	4.4	5.0
E. Controls.....				.72	.75

Thyroid containing 0.106, 0.148, and 0.3 per cent iodine, respectively, was fed to mice. When fed in amounts corresponding to the ratio of 3, 2, and 1 (namely, in the inverse ratio to the iodine content) the physiological effects were approximately equal. With equal amounts of the thyroid containing 0.148 and 0.3 per cent iodine the latter was much the more active.

SERIES III.

In the following experiments the effects of the thyroid of Group 3 (normal; 0.106 per cent iodine) and of Group 5 (iodoform fed dogs; 0.3 per cent iodine) were compared.

A. THYROID OF GROUP 3 (NORMAL); 0.106 PER CENT IODINE.

Date.	Weight.	Remarks.
1908.		
April 25.....	18.45	Feeding of cakes each containing 0.0005 gm. thyroid commenced.
29.....	19.74	
May 2.....	19.74	Acetonitrile, 35.53 mgms., i. e., 1.8 mgms. per gm. mouse. Survived.
3.....	19.74	
April 25.....	15.00	Thyroid as above.
29.....	15.16	
May 2.....	15.14	Acetonitrile, 29.03 mgms., i. e., 1.9 mgms. per gm. mouse. Survived.
4.....	15.28	
5.....		
April 25.....	15.73	Thyroid as above.
29.....	14.88	
May 2.....	14.50	Acetonitrile, 30.11 mgms., i. e., 2.1 mgms. per gm. mouse. Died 6 hours.
4.....	14.34	
April 25.....	16.87	Thyroid as above.
29.....	18.20	
May 2.....	17.60	Acetonitrile, 41.75 mgms., i. e., 2.3 mgms. per gm. mouse. Died 3½ hours.
4.....	18.15	

B. THYROID OF GROUP 3 (NORMAL); 0.106 PER CENT IODINE.

Date.	Weight.	Remarks.
1908.		
April 25.....	13.75	Feeding of cakes each containing 0.0015 gm. thyroid commenced.
29.....	14.34	
May 2.....	14.92	Acetonitrile, 37.3 mgms., i. e., 2.5 mgms. per gm. mouse. Survived.
3.....	14.92	
April 25.....	14.20	Thyroid as above.
29.....	14.30	
May 2.....	13.48	Acetonitrile, 41.17 mgms., i. e., 3.1 mgms. per gm. mouse. Survived.
4.....	13.28	
April 25.....	16.32	Thyroid as above.
29.....	15.28	
May 2.....	15.32	Acetonitrile, 52.85 mgms., i. e., 3.6 mgms. per gm. mouse. Died 1½ hours.
4.....	14.68	
5.....		
April 25.....	16.23	Thyroid as above.
29.....	17.68	
May 2.....	17.34	Acetonitrile, 61.86 mgms., i. e., 3.8 mgms. per gm. mouse. Died 50 hours.
4.....	16.28	

C. THYROID OF GROUP 5 (IODOFORM FED DOGS); 0.3 PER CENT IODINE.

1908.		
April 25.....	14.93	Feeding of cakes each containing 0.0005 gm. thyroid commenced.
29.....	16.50	
May 2.....	16.84	Acetonitrile, 45.47 mgms., i. e., 2.7 mgms. per gm. mouse. Survived.
3.....	16.84	
April 25.....	15.99	Thyroid as above.
29.....	16.64	
May 2.....	16.32	Acetonitrile, 51.27 mgms., i. e., 3.1 mgms. per gm. mouse. Survived.
4.....	16.54	
April 25.....	15.49	Thyroid as above.
29.....	16.37	
May 2.....	12.96	Acetonitrile, 52.72 mgms., i. e., 3.7 mgms. per gm. mouse. Survived.
4.....	14.25	
April 25.....	15.13	Thyroid as above.
29.....	15.64	
May 2.....	14.75	Acetonitrile, 61.82 mgms., i. e., 4.2 mgms. per gm. mouse. Died 1½ hours.
4.....	14.72	
5.....		

D. THYROID OF GROUP 5.

1908.		
April 25.....	15.05	Feeding of cakes each containing 0.001 gm. thyroid commenced.
29.....	16.08	
May 2.....	15.66	Acetonitrile, 46.98 mgms., i. e., 3 mgms. per gm. mouse. Survived.
3.....	15.66	
April 25.....	14.84	Thyroid as above.
29.....	15.44	
May 2.....	14.24	Acetonitrile, 50.94 mgms., i. e., 3.6 mgms. per gm. mouse. Survived
4.....	14.15	
April 25.....	15.24	Thyroid as above.
29.....	15.00	
May 2.....	14.83	Acetonitrile, 60.23 mgms., i. e., 4.1 mgms. per gm. mouse. Survived.
4.....	14.69	
April 25.....	15.54	Thyroid as above.
29.....	16.04	
May 2.....	16.16	Acetonitrile, 74.26 mgms., i. e., 4.7 mgms. per gm. mouse. Died 4½ hours.
4.....	15.80	
5.....		

E. CONTROLS.

Date.	Weight.	Remarks.
1908.		
April 25.....	13.45	Feeding of cakes without thyroid commenced.
29.....	14.47	
May 2.....	14.56	Acetonitrile, 7.43 mgms., i. e., 0.51 mgm. per gm. mouse. Survived.
3.....	14.56	
April 25.....	18.43	Cakes as above.
29.....	19.67	
May 2.....	19.76	Acetonitrile, 10.16 mgms., i. e., 0.52 mgm. per gm. mouse. Died 1 hour.
4.....	19.54	
5.....		
April 25.....	16.88	Cakes as above.
29.....	15.43	
May 2.....	15.57	Acetonitrile, 8.06 mgms., i. e., 0.53 mgm. per gm. mouse. Died 8 hours.
4.....	15.21	
5.....		

Summary.—The results of the above experiments may be tabulated as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.0005	0.106	0.00053	1.9	2.1
B.....	.0015	.106	.00159	3.1	3.6
C.....	.0005	.300	.00150	3.7	4.2
D.....	.001	.300	.00300	4.1	4.7
E. Controls.....				.51	.52

With equal amounts of thyroid containing, respectively, 0.106 and 0.3 per cent iodine, the effect of the latter was much greater than that of the former; with three parts of the former and one part of the latter the effects were nearly equal. One part of the thyroid rich in iodine was also much more active than one and one-half parts of the thyroid poor in iodine.

SERIES IV.

In this series equal amounts of the thyroid of Groups 2 and 1 (normal) and of Group 5 (iodoform fed dogs) were compared.

A. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
May 9.....	13.83	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
16.....	12.49	
18.....	11.76	Acetonitrile, 12.94 mgms., i. e., 1.1 mgms. per gm. mouse. Survived.
May 9.....	18.52	Thyroid as above.
16.....	18.43	
18.....	18.29	Acetonitrile, 26.61 mgms., i. e., 1.4 mgms. per gm. mouse. Died 5 hours.
May 9.....	18.48	Thyroid as above.
16.....	19.00	
17.....		Acetonitrile, 34.2 mgms., i. e., 1.8 mgms. per gm. mouse. Died 2 hours.
May 9.....	14.98	Thyroid as above.
16.....	12.80	
17.....		Acetonitrile, 32.0 mgms., i. e., 2.5 mgms. per gm. mouse. Died 3 hours.

B. THYROID OF GROUP 1 (NORMAL); 0.129 PER CENT IODINE.

1908.		
May 9.....	16.17	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
15.....	16.84	
18.....	16.71	Acetonitrile, 26.74 mgms., i. e., 1.6 mgms. per gm. mouse. Survived.
May 9.....	11.50	Thyroid as above.
15.....	12.67	
16.....	12.46	
18.....	12.59	Acetonitrile, 22.62 mgms., i. e., 1.8 mgms. per gm. mouse. Survived.
May 9.....	15.87	Thyroid as above.
15.....	15.17	
16.....	14.87	
17.....		Acetonitrile, 31.23 mgms., i. e., 2.1 mgms. per gm. mouse. Died 1½ hours.
May 9.....	15.71	Thyroid as above.
15.....	14.61	
16.....	14.58	
17.....		Acetonitrile, 36.45 mgms., i. e., 2.5 mgms. per gm. mouse. Died 1½ hours.

C. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

1908.		
May 9.....	21.46	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
16.....	19.13	
18.....	19.15	Acetonitrile, 55.54 mgms., i. e., 2.9 mgms. per gm. mouse. Survived.
May 9.....	14.50	Thyroid as above.
16.....	13.39	
17.....		Acetonitrile, 41.51 mgms., i. e., 3.1 mgms. per gm. mouse. Survived..
May 9.....	16.12	Thyroid as above.
16.....	15.02	
18.....	15.05	Acetonitrile, 49.66 mgms., i. e., 3.3 mgms. per gm. mouse. Died 2½ hours.
May 9.....	14.26	Thyroid as above.
16.....	12.25	Acetonitrile, 42.88 mgms., i. e., 3.5 mgms. per gm. mouse. Died 4½ hours.

D. (CONTROLS.)

Date.	Weight of mouse.	Remarks.
1908.		
May 9.....	16.65	Feeding of cakes without thyroid commenced.
15.....	16.06	
16.....	16.05	
17.....		Acetonitrile, 5.78 mgms., i. e., 0.36 mgm. per gm. mouse. Survived.
May 9.....	16.50	Cakes as above.
15.....	15.74	
16.....	15.42	
18.....	15.56	Acetonitrile, 5.76 mgms., i. e., 0.37 mgm. per gm. mouse. Died 2 hours.
May 9.....	15.79	Cakes as above.
15.....	11.80	
16.....	12.15	
18.....	13.16	Acetonitrile, 5.27 mgms., i. e. 0.4 mgm. per gm. mouse. Died 4 hours.

Summary.—The results of the above experiments may be summarized as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.0005	0.111	0.00055	1.1	1.4
B.....	.0005	.129	.00064	1.8	2.1
C.....	.0005	.300	.00150	3.1	3.3
D. Controls.....				.36	.37

The thyroid of the dogs which had received iodoform was much more active than that of the normal dogs.

b. EXPERIMENTS ON RATS.

Results very similar to the above were obtained in a series of experiments upon rats. In these animals there is a diminution of resistance to acetonitrile.

A. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
May 15.....	32	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
18.....	33	
20.....	33	
23.....	32	Acetonitrile, 51.2 mgms., i. e., 1.6 mgms. per gm. rat. Died about 17 hours.
May 15.....	43	Thyroid as above.
18.....	43	
20.....	43	
23.....	41	
24.....		Acetonitrile, 73.8 mgms., i. e., 1.8 mgms. per gm. rat. Survived.
May 15.....	50	Thyroid as above.
18.....	50	
20.....	46	
23.....	48	Acetonitrile, 100.8 mgms., i. e., 2.1 mgms. per gm. rat. Died 2 hours.
May 15.....	35	Thyroid as above.
18.....	34	
20.....	34	
23.....	32	
25.....	32	Acetonitrile, 70.4 mgms., i. e., 2.2 mgms. per gm. rat. Died 4 hours.

B. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
May 15.....	36	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
18.....	37	
20.....	37	
23.....	34	Acetonitrile, 34 mgms., i. e., 1 mgm. per gm. rat. Survived.
May 15.....	44	Thyroid as above.
18.....	42	
20.....	43	
23.....	41	
24.....	41	Acetonitrile, 53.3 mgms., i. e., 1.3 mgms. per gm. rat. Survived.
May 15.....	38	Thyroid as above.
18.....	37	
20.....	36	
23.....	35	Acetonitrile, 52.5 mgms., i. e., 1.5 mgms. per gm. rat. Died 1½ hours.

C. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

1908.		
May 15.....	41	Feeding of cakes, each containing 0.0015 gm. thyroid, commenced.
18.....	39	
20.....	38	
23.....	38	Acetonitrile, 45.6 mgms., i. e., 1.2 mgms. per gm. rat. Survived.
May 15.....	43	Thyroid as above.
18.....	41	
20.....	41	
23.....	38	
24.....		Acetonitrile, 49.4 mgms., i. e., 1.3 mgms. per gm. rat. Died 1 hour.
May 15.....	36	Thyroid as above.
18.....	35	
20.....	34	
23.....	33	
24.....		Acetonitrile, 46.2 mgms., i. e., 1.4 mgms. per gm. rat. Died 4 to 7 hours.
May 15.....	64	Thyroid as above.
18.....	57	
20.....	59	
23.....	58	Acetonitrile, 92.8 mgms., i. e., 1.6 mgms. per gm. rat. Died 3 hours.

D. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

1908.		
May 15.....	38	Feeding of cakes, each containing 0.003 gm. thyroid, commenced.
18.....	37	
20.....	36	
23.....	35	Acetonitrile, 28 mgms., i. e., 0.8 mgm. per gm. rat. Survived.
May 15.....	45	Thyroid as above.
18.....	43	
20.....	43	
23.....	41	
24.....	41	Acetonitrile 36.9 mgms., i. e., 0.9 mgm. per gm. rat. Survived.
May 15.....	37	Thyroid as above.
18.....	35	
20.....	37	
23.....	34	
24.....		Acetonitrile, 34 mgms., i. e., 1 mgm. per gm. rat. Died 1 hour.
May 15.....	31	Thyroid as above.
18.....	31	
20.....	31	
23.....	29	Acetonitrile, 31.9 mgms., i. e., 1.1 mgms. per gm. rat. Died 2½ hours.

E. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
May 15.....	43	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
18.....	36	
20.....	37	
23.....	36	
24.....	36	Acetonitrile, 18 mgms., i. e., 0.5 mgm. per gm. rat. Survived.
May 15.....	38	Thyroid as above.
18.....	37	
20.....	38	
23.....	35	
24.....		Acetonitrile, 21 mgms., i. e., 0.6 mgm. per gm. rat. Died 1 to 2 hours.
May 15.....	36	Thyroid as above.
18.....	34	
20.....	35	
23.....	33	Acetonitrile, 23.1 mgms., i. e., 0.7 mgm. per gm. rat. Died 4½ hours.
May 15.....	41	Thyroid as above.
18.....	38	
20.....	38	
23.....	35	Acetonitrile, 35 mgms., i. e., 1 mgm. per gm. rat. Died 2½ hours.

F. CONTROLS.

1908.		
May 15.....	41	Feeding of cakes without thyroid commenced.
18.....	38	
20.....	37	
23.....	38	Acetonitrile, 87.4 mgms., i. e., 2.3 mgms. per gm. rat. Survived.
May 15.....	41	Cakes as above.
18.....	39	
20.....	37	
23.....	36	Acetonitrile, 100.8 mgms., i. e., 2.8 mgms. per gm. rat. Survived.
May 15.....	50	Cakes as above.
18.....	46	
20.....	48	
23.....	44	
24.....		Acetonitrile, 127.6 mgms. i. e., 2.9 mgms. per gm. rat. Survived.
May 15.....	69	Cakes as above.
18.....	64	
20.....	65	
23.....	62	
24.....		Acetonitrile, 186 mgms., i. e., 3 mgms. per gm. rat. Died 2½ hours.
May 15.....	42	Cakes as above.
18.....	38	
20.....	38	
23.....	37	Acetonitrile, 114.7 mgms., i. e., 3.1 mgms. per gm. rat. Died 3 to 6 hours.

Summary.—The results of the above experiments may be tabulated as follows:

	Gm. thyroid in each cake.	Percentage of iodine in thyroid.	Mm. I in thyroid of each cake.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.0005	0.111	0.00055	1.8	2.1
B.....	.0005	.300	.00150	1.3	1.5
C.....	.0015	.111	.00166	1.2	1.3
D.....	.003	.111	.00333	.9	1.0
E.....	.001	.300	.00300	.5	.6
F. Controls.....				2.9	3.0

With equal amounts of thyroid that containing the higher percentage of iodine was the more active. To obtain approximately equal effects it was necessary to give three times as much of the thyroid poor in iodine as of the thyroid rich in iodine.

2. EXPERIMENTS WITH MORPHINE.

a. EXPERIMENTS ON MICE.

Only one short series of experiments was performed in which the effect of feeding the above thyroid preparations upon the resistance of mice to morphine sulphate was tested.

The results indicate that the thyroid of the iodoform-fed dogs is distinctly more active in lowering the resistance of mice to morphine than is that of the normal dogs.

A. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1907.		
July 3.....	11.64	Feeding of cakes, each containing 0.01 gm. thyroid, commenced.
8.....	11.74	
11.....	11.10	
13.....	10.40	
		Morphine sulphate, 0.73 mgms., i. e., 0.07 mgm. per gm. mouse. Survived
July 3.....	13.33	Thyroid as above.
8.....	13.64	
11.....	14.45	
14.....	13.88	
		Morphine sulphate, 1.47 mgms., i. e., 0.11 mgm. per gm. mouse. Survived.
July 3.....	12.14	Thyroid as above.
8.....	12.77	
11.....	12.05	
13.....	11.25	
		Morphine sulphate, 1.8 mgms., i. e., 0.16 mgm. per gm. mouse. Died three-fourths hour.

B. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

1907.		
July 3.....	14.65	Feeding of cakes, each containing 0.01 gm. thyroid, commenced.
8.....	16.22	
12.....	13.00	
14.....	11.76	
		Morphine sulphate, 0.82 mgm., i. e., 0.07 mgm. per gm. mouse. Survived.
July 3.....	12.62	Thyroid as above.
8.....	13.02	
12.....	13.32	
14.....	11.94	
		Morphine sulphate, 1.07 mgms., i. e., 0.09 mgm. per gm. mouse. Survived.
July 3.....	13.23	Thyroid as above.
8.....	13.10	
12.....	12.45	
13.....	12.32	
		Morphine sulphate, 1.23 mgms., i. e., 0.1 mgm. per gm. mouse. Died 2 hours

C. CONTROLS.

Date.	Weight of mouse.	Remarks.
1907.		
July 3.....	13.30	Feeding of cakes without thyroid commenced.
8.....	14.40	
12.....	14.25	Morphine sulphate, 5.27 mgms., i. e., 0.37 mgm. per gm. mouse. Survived.
July 3.....	11.40	Cakes as above.
8.....	11.90	
12.....	12.45	
13.....	12.33	Morphine sulphate, 5.18 mgms., i. e., 0.42 mgm. per gm. mouse. Survived.
July 3.....	14.25	Cakes as above.
8.....	14.46	
12.....	14.85	
14.....	14.40	Morphine sulphate, 6.19 mgms., i. e., 0.43 mgm. per gm. mouse. Survived.
July 3.....	12.90	Cakes as above.
8.....	15.32	
12.....	15.72	
15.....	15.40	Morphine sulphate, 6.93 mgms., i. e., 0.45 mgm. per gm. mouse. Died 1½ hours
July 3.....	13.85	Cakes as above.
8.....	12.90	
12.....	11.77	
14.....	11.75	Morphine sulphate, 5.4 mgms., i. e., 0.46 mgm. per gm. mouse. Died about 2 hours.

Summary.—The results of these experiments may be tabulated as follows:

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mg. I in thyroid fed daily.	Fatal dose of morphine sulphate in mgm. per gm.	
				Recovered.	Died.
A.....	0.01	0.111	0.0111	0.11	0.16
B.....	.01	.300	.0300	.09	.10
C. Controls.....				.43	.45

b. EXPERIMENTS ON RATS.

The following series of experiments on rats, although very incomplete, show that the activity of the thyroid, the iodine content of which has been increased by the administration of iodoform to dogs, was much greater than that of normal thyroid.

SERIES I.

A. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
May 15.....	43	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
18.....	43	
20.....	43	
23.....	41	
27.....	40	Morphine sulphate, 10 mgms., i. e., 0.25 mgm. per gm. rat. Survived.

B. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

Date.	Weight of rat.	Remarks.
1908.		
May 15.....	36	Feeding of cakes, each containing 0.0005 gm. thyroid, commenced.
18.....	37	
20.....	37	
23.....	34	
25.....	34	Morphine sulphate, 4.76 mgms., i. e., 0.14 mgm. per gm. rat. Survived.
May 15.....	41	Thyroid as above.
18.....	39	
20.....	40	
23.....	39	
26.....	35	Morphine sulphate, 7. mgms., i. e., 0.2 mgm. per gm. rat. Survived.
May 15.....	44	Thyroid as above.
18.....	42	
20.....	43	
23.....	41	
24.....	41	
28.....	43	Morphine sulphate, 10.75 mgms., i. e., 0.25 mgm. per gm. rat. Died 5 hours.

C. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

1908.		
May 15.....	41	Feeding of cakes, each containing 0.0015 gm. thyroid, commenced.
18.....	39	
20.....	38	
23.....	38	
27.....	40	Morphine sulphate, 10 mgms., i. e., 0.25 mgm. per gm. rat. Died 2½ hours.

D. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

1908.		
May 15.....	38	Feeding of cakes, each containing 0.003 gm. thyroid, begun.
18.....	37	
20.....	36	
23.....	35	
26.....	40	Morphine sulphate, 6.4 mgms., i. e., 0.16 mgm. per gm. rat. Survived.
May 15.....	45	Thyroid as above.
18.....	43	
20.....	43	
23.....	41	
24.....	41	
28.....	43	Morphine sulphate, 8.6 mgms., i. e., 0.2 mgm. per gm. rat. Died 3½ hours.

E. THYROID OF GROUP 3 (NORMAL); 0.106 PER CENT IODINE.

1908.		
May 15.....	54	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
18.....	52	
20.....	51	
23.....	50	
24.....	50	
27.....	51	Morphine sulphate, 12.75 mgms., i. e., 0.25 mgm. per gm. rat. Survived.

F. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

1908.		
May 15.....	43	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
18.....	36	
20.....	37	
23.....	36	
24.....	36	
27.....	37	Morphine sulphate, 7.4 mgms., i. e., 0.2 mgm. per gm. rat. Died 5 hours.

G. CONTROLS.

Date.	Weight of rat.	Remarks.
1908.		
May 15.....	41	Feeding of cakes without thyroid commenced.
18.....	38	
20.....	37	
23.....	38	
26.....	40	
		Morphine sulphate, 13.6 mgms., i. e., 0.34 mgm. per gm. rat. Survived.
May 15.....	41	Cakes as above.
18.....	39	
20.....	37	
23.....	36	
28.....	36	
		Morphine sulphate, 14 mgms., i. e., 0.39 mgm. per gm. rat. Survived.
May 15.....	50	Cakes as above.
18.....	46	
20.....	48	
23.....	44	
27.....	44	
		Morphine sulphate, 17.6 mgms., i. e., 0.4 mgm. per gm. rat. Died 4 hours.

Summary.—These experiments may be summarized as follows:

	Gm. thy- roid in each cake.	Percentage of iodine in thyroid.	Mgm. I in thyroid of each cake.	Loss of weight in per cent of original weight.	Fatal dose of mor- phine sulphate in mgm. per gm.	
					Recovered.	Died.
A.....	0.0005	0.111	0.00055	7.0	0.25
B.....	.0005	.3	.0015	7.6	.20	0.25
C.....	.0015	.111	.00166	2.425
D.....	.003	.111	.00333	.0	.16	.20
E.....	.001	.106	.00106	5.5	.25
F.....	.001	.3	.0030	14.020
G. Controls.....	9.1	.39	.40

These experiments show that with equal amounts of thyroid containing different percentages of iodine those with the larger amounts of iodine caused the greater lowering of resistance to morphine; also that in order to obtain equal physiological effects it was necessary to feed much more of the iodine-poor thyroid. Loss of weight can not explain the increased susceptibility of the rats to morphine, for with but one exception there was no loss of weight greater than that which could be ascribed to the exclusive cracker diet.

SERIES B.

Twenty-three dogs were divided into three groups. There were six dogs in the first group (Group 6), nine in the second (Group 7), and eight in the third (Group 8). Each of the dogs of Group 6 received about 1.2 grams iodoform in capsules on two successive days; they were killed on the day following that on which they had received the second dose. The glands were weighed and dried as described under Series A.

Group.	Weight of thyroid fresh.	Weight of thyroid dried.	Per cent of water.	Per cent of iodine.
6 (iodoform).....	12.40	3.20	74.2	0.21
7 (normal).....	33.05	8.69	73.7	.10
8 (normal).....	17.40	4.60	73.5	.12

The following experiments were performed with these thyroids and some of those of Series A.

A. THYROID OF GROUP 8 (NORMAL); 0.12 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
July 13.....	19.13	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
17.....	17.18	
21.....	17.80	Acetonitrile, 8.01 mgms., i. e., 0.45 mgm. per gm. mouse. Survived.
July 13.....	16.40	Thyroid as above.
17.....	15.89	
21.....	15.66	Acetonitrile, 8.61 mgms., i. e., 0.55 mgm. per gm. mouse. Died 1 hour.
July 13.....	14.51	Thyroid as above.
17.....	14.09	
21.....	12.73	Acetonitrile, 8.91 mgms., i. e., 0.7 mgm. per gm. mouse. Died 2½ hours.

B. THYROID OF GROUP 2 (NORMAL); 0.111 PER CENT IODINE.

1908.		
July 13.....	15.36	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
17.....	13.78	
21.....	12.45	Acetonitrile, 8.09 mgms., i. e., 0.65 mgm. per gm. mouse. Died about 4 hours.
July 13.....	12.81	Thyroid as above.
17.....	11.59	
21.....	11.25	Acetonitrile, 10.13 mgms., i. e., 0.9 mgm. per gm. mouse. Died 1 hour.

C. THYROID OF GROUP 6 (IODOFORM); 0.21 PER CENT IODINE.

1908.		
July 13.....	14.00	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
17.....	13.25	
21.....	12.17	Acetonitrile, 10.95 mgms., i. e., 0.9 mgm. per gm. mouse. Survived.
July 13.....	11.80	Thyroid as above.
17.....	10.59	
21.....	11.29	Acetonitrile, 15.81 mgms., i. e., 1.4 mgms. per gm. mouse. Survived.
July 13.....	13.78	Thyroid as above.
17.....	14.14	
21.....	14.30	Acetonitrile, 22.88 mgms., i. e., 1.6 mgms. per gm. mouse. Survived.
July 13.....	12.25	Thyroid as above.
17.....	12.36	
21.....	9.84	Acetonitrile, 18.70 mgms., i. e., 1.9 mgms. per gm. mouse. Died 1 hour.

D. THYROID OF GROUP 5 (IODOFORM); 0.3 PER CENT IODINE.

Date.	Weight of mouse.	Remarks.
1908.		
July 13.....	15.91	Feeding of cakes, each containing 0.001 gm. thyroid, commenced.
17.....	14.88	
21.....	14.90	Acetonitrile, 19.37 mgms., i. e., 1.3 mgms. per gm. mouse. Survived.
July 13.....	17.39	Thyroid as above.
17.....	16.33	
21.....	16.20	Acetonitrile, 30.78 mgms., i. e., 1.9 mgms. per gm. mouse. Survived.
July 13.....	14.52	Thyroid as above.
17.....	13.72	
21.....	12.63	
22.....		Acetonitrile, 26.52 mgms., i. e., 2.1 mgms. per gm. mouse. Survived.
July 13.....	17.78	Thyroid as above.
17.....	16.40	
21.....	17.12	Acetonitrile, 41.09 mgms., i. e., 2.4 mgms. per gm. mouse. Died 3 hours.

E. CONTROLS.

1908.		
July 13.....	14.35	Feeding of cakes without thyroid commenced.
17.....	13.98	
21.....	13.53	Acetonitrile, 3.25 mgms., i. e., 0.24 mgm. per gm. mouse. Survived.
July 13.....	13.25	Cakes as above.
17.....	12.83	
21.....	12.96	Acetonitrile, 3.24 mgms., i. e., 0.25 mgm. per gm. mouse. Died 1 hour.
July 13.....	14.20	Cakes as above.
17.....	13.03	
21.....	11.50	
22.....		Acetonitrile, 2.99 mgms., i. e., 0.26 mgm. per gm. mouse. Died 2½ hours.

SUMMARY.

	Gm. thyroid fed daily.	Percentage of iodine in thyroid.	Mgm. I in thyroid fed daily.	Fatal dose of acetonitrile in mgms. per gm.	
				Recovered.	Died.
A.....	0.001	0.12	0.0012	0.45	0.55
B.....	.001	.111	.00111		.65
C.....	.001	.21	.0021	1.6	1.9
D.....	.001	.3	.0030	2.1	2.4
E, Controls.....				.24	.25

The results are very similar to those obtained with the thyroid of Series A. The thyroid, the iodine content of which had been increased by the administration of iodoform, was much more active in protecting mice against acetonitrile than was that of the normal dogs.

GENERAL SUMMARY OF ABOVE EXPERIMENTS AND CONCLUSIONS.

The experiments described above show that when potassium iodide or iodoform is administered to dogs the thyroids of the latter contain a greatly increased percentage of iodine and also are much more active physiologically. This result occurred too quickly to admit of any explanation other than that the increased activity was due to the increased iodine content. It seems to us to show conclusively that thyroid rich in iodine is more active than thyroid poor in iodine simply on account of the iodine; in other words, that the iodine is the cause and not the result of the activity.

LIST OF HYGIENIC LABORATORY BULLETINS OF THE PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.

The Hygienic Laboratory was established in New York, at the Marine Hospital on Staten Island, August, 1887. It was transferred to Washington, with quarters in the Butler Building, June 11, 1891, and a new laboratory building, located in Washington, was authorized by act of Congress, March 3, 1901.

The following *bulletins* [Bulls. Nos. 1-7, 1900 to 1902, Hyg. Lab., U. S. Mar.-Hosp. Serv., Wash.] have been issued:

*No. 1.—Preliminary note on the viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 2.—Formalin disinfection of baggage without apparatus. By M. J. Rosenau.

*No. 3.—Sulphur dioxid as a germicidal agent. By H. D. Geddings.

*No. 4.—Viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 5.—An investigation of a pathogenic microbe (*B. typhi murium* Danyz.) applied to the destruction of rats. By M. J. Rosenau.

*No. 6.—Disinfection against mosquitoes with formaldehyd and sulphur dioxid, By M. J. Rosenau.

No. 7.—Laboratory technique: Ring test for indol, by S. B. Grubbs and Edward Francis; Collodium sacs, by S. B. Grubbs and Edward Francis; Microphotography with simple apparatus, by H. B. Parker.

By act of Congress approved July 1, 1902, the name of the "United States Marine-Hospital Service" was changed to the "Public Health and Marine-Hospital Service of the United States," and three new divisions were added to the Hygienic Laboratory.

Since the change of name of the Service the bulletins of the Hygienic Laboratory have been continued in the same numerical order, as follows:

*No. 8.—Laboratory course in pathology and bacteriology. By M. J. Rosenau. (Revised edition, March, 1904.)

*No. 9.—Presence of tetanus in commercial gelatin. By John F. Anderson.

No. 10.—Report upon the prevalence and geographic distribution of hookworm disease (uncinariasis or ancylostomiasis) in the United States. By Ch. Wardell Stiles.

*No. 11.—An experimental investigation of *Trypanosoma lewisi*. By Edward Francis.

*No. 12.—The bacteriological impurities of vaccine virus; an experimental study. By M. J. Rosenau.

*No. 13.—A statistical study of the intestinal parasites of 500 white male patients at the United States Government Hospital for the Insane; by Philip E. Garrison, Brayton H. Ransom, and Earle C. Stevenson. A parasitic roundworm (*Agamomermis culicis* n. g., n. sp.) in American mosquitoes (*Culex sollicitans*); by Ch. Wardell Stiles. The type species of the cestode genus *Hymenolepis*; by Ch. Wardell Stiles.

No. 14.—Spotted fever (tick fever) of the Rocky Mountains; a new disease. By John F. Anderson.

No. 15.—Inefficiency of ferrous sulphate as an antiseptic and germicide. By Allan J. McLaughlin.

*No. 16.—The antiseptic and germicidal properties of glycerin. By M. J. Rosenau.

*No. 17.—Illustrated key to the trematode parasites of man. By Ch. Wardell Stiles.

*No. 18.—An account of the tapeworms of the genus *Hymenolepis* parasitic in man, including reports of several new cases of the dwarf tapeworm (*H. nana*) in the United States. By Brayton H. Ransom.

*No. 19.—A method for inoculating animals with precise amounts. By M. J. Rosenau.

*No. 20.—A zoological investigation into the cause, transmission, and source of Rocky Mountain "spotted fever." By Ch. Wardell Stiles.

No. 21.—The immunity unit for standardizing diphtheria antitoxin (based on Ehrlich's normal serum). Official standard prepared under the act approved July 1, 1902. By M. J. Rosenau.

*No. 22.—Chloride of zinc as a deodorant, antiseptic, and germicide. By T. B. McClintic.

*No. 23.—Changes in the Pharmacopœia of the United States of America. Eighth Decennial Revision. By Reid Hunt and Murray Galt Motter.

No. 24.—The International Code of Zoological Nomenclature as applied to medicine. By Ch. Wardell Stiles.

No. 25.—Illustrated key to the cestode parasites of man. By Ch. Wardell Stiles.

No. 26.—On the stability of the oxidases and their conduct toward various reagents. The conduct of phenolphthalein in the animal organism. A test for saccharin, and a simple method of distinguishing between cumarin and vanillin. The toxicity of ozone and other oxidizing agents to lipase. The influence of chemical constitution on the lipolytic hydrolysis of ethereal salts. By J. H. Kastle.

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No. 30.—I. Maternal transmission of immunity to diphtheria toxine. II. Maternal transmission of immunity to diphtheria toxine and hypersusceptibility to horse serum in the same animal. By John F. Anderson.

No. 31.—Variations in the peroxidase activity of the blood in health and disease. By Joseph H. Kastle and Harold L. Amoss.

No. 32.—A stomach lesion in guinea pigs caused by diphtheria toxine and its bearing upon experimental gastric ulcer. By M. J. Rosenau and John F. Anderson.

No. 33.—Studies in experimental alcoholism. By Reid Hunt.

No. 34.—I. *Agamofilaria georgiana* n. sp., an apparently new roundworm parasite from the ankle of a negress. II. The zoological characters of the roundworm genus *Filaria* Mueller, 1787. III. Three new American cases of infection of man with horse-hair worms (species *Paragordius varius*), with summary of all cases reported to date. By Ch. Wardell Stiles.

*No. 35.—Report on the origin and prevalence of typhoid fever in the District of Columbia. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle. (Including articles contributed by Ch. Wardell Stiles, Joseph Goldberger, and A. M. Stimson.)

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No. 37.—Index-catalogue of medical and veterinary zoology. Subjects: Trematoda and trematode diseases. By Ch. Wardell Stiles and Albert Hassall.

No. 38.—The influence of antitoxin upon post-diphtheritic paralysis. By M. J. Rosenau and John F. Anderson.

No. 39.—The antiseptic and germicidal properties of solutions of formaldehyde and their action upon toxins. By John F. Anderson.

No. 40.—1. The occurrence of a proliferating cestode larva (*Sparganum proliferum*) in man in Florida, by Ch. Wardell Stiles. 2. A reexamination of the type specimen of *Filaria restiformis* Leidy, 1880=*Agamomermis restiformis*, by Ch. Wardell Stiles. 3. Observations on two new parasitic trematode worms: *Homalogaster philippinensis*

n. sp., *Agamodistomum nanus* n. sp., by Ch. Wardell Stiles and Joseph Goldberger.
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*No. 41.—Milk and its relation to the public health. By various authors.

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No. 43.—The standardization of tetanus antitoxin (an American unit established under authority of the act of July 1, 1902). By M. J. Rosenau and John F. Anderson.

No. 44.—Report No. 2 on the origin and prevalence of typhoid fever in the District of Columbia, 1907. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle.

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No. 46.—*Hepatozoon perniciosum* (n. g., n. sp.); a hæmogregarine pathogenic for white rats; with a description of the sexual cycle in the intermediate host, a mite (*Ielaps echidninus*). By W. W. Miller.

No. 47.—Studies on Thyroid: I. The relation of iodine to the physiological activity of thyroid preparations. By Reid Hunt and Atherton Seidell.

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TREASURY DEPARTMENT
Public Health and Marine-Hospital Service of the United States

HYGIENIC LABORATORY.—BULLETIN No. 48

DECEMBER, 1908

THE PHYSIOLOGICAL STANDARD- IZATION OF DIGITALIS

By

CHARLES WALLIS EDMUNDS

and

WORTH HALE



WASHINGTON
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CONTENTS.

	Page.
1. Introduction.....	7
2. Chemistry of digitalis.....	7
3. Relationship of digitoxin content to physiological activity.....	8
4. Variability of digitalis preparations.....	10
5. Literature relating to standardization methods.....	16
6. Summary of standardization literature.....	31
7. Preparations of digitalis assayed.....	32
8. Methods employed with—	
(a) Results.....	34
(b) Discussion of factors involved.....	40
(c) Summary of results obtained.....	49
9. Discussion of results.....	51
10. Report on the preparations examined.....	54

THE PHYSIOLOGICAL STANDARDIZATION OF DIGITALIS.^a

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One of the directions along which scientific medicine has advanced during the past few years is in the greater accuracy with which medicines are administered. A very essential factor in this tendency is that the drugs themselves shall be of a uniform strength, and to insure this the Pharmacopœia of the United States, in its last revision, provided a number of standards to which official preparations must conform. Especially is this true in the case of a number of drugs, such as opium, belladonna, nux vomica, etc., in which the active constituents are capable of isolation in a pure form. With a considerable number of others, however, this was not found to be possible for the reason that the active principles are either not known or are not capable of being isolated in pure state by any known chemical method. In this class occur such drugs in common use as digitalis and the other members of that series, ergot and cannabis indica.

By far the most important member of this group is digitalis itself, on account of its widespread use in cases of cardiac disease. At the present time it is impossible to secure a standardized preparation of the drug by any known chemical means^b on account of the fact that the activity of the drug depends upon no single active principle, but upon several whose chemistry is not completely known and for the isolation of which there does not, at the present time, exist any satisfactory chemical method.

Our knowledge of the chemistry of the digitalis leaves we owe mainly to Schmiedeberg and Kiliani. The most important constituent is digitoxin, a glucoside, which is insoluble in water but soluble

^a Submitted for publication December 4, 1908.

^b Some firms put out preparations standardized so as to contain a certain percentage of digitoxin, but, as will be pointed out, this need not indicate a uniform physiological activity.

in alcohol and chloroform. In watery solutions of the drug it is probably made soluble by the presence of other constituents of the plant, most likely the saponin-like body, digitonin. The digitoxin is readily broken up into digitoxigenin and the sugar, digitoxose. Schmiedeberg obtained toxiresin as a decomposition product, a body which is related in action to the picrotoxin group.

A second glucoside is digitalinum verum or digitalin, which is soluble in alcohol but insoluble in chloroform or water. This breaks up into an inactive body digitaligenin and two sugars. The digitalinum verum is found mainly in the seeds.

Digitalein^a resembles digitalin very closely, differing from it, however, in being soluble in water.

Digitophyllin, another glucoside, which has been isolated, resembles digitoxin.

While digitoxin is the most important constituent of the preparations of digitalis it does not necessarily follow that the activity of the drug runs parallel with the digitoxin content. At least this is true as far as we can judge by the method which is available for the isolation of this body, viz, the Keller method or the Keller method as modified by Fromme. Keller's method^b for the isolation of digitoxin consists in the extraction of a certain amount of carefully dried and powdered leaves with dilute alcohol. The percolate is evaporated to drive off the alcohol and the residue is taken up with water and lead acetate added. A voluminous precipitate results, but only the first portion of the filtrate obtained is saved to avoid the uncertainty of attempting to wash the precipitate free from digitoxin. Sodium sulphate is added to the filtrate to precipitate any excess of lead and after standing four to five hours the clear liquid is decanted, made alkaline with ammonia, and shaken out with chloroform. The chloroformic solution is evaporated and a yellow resinous mass, the digitoxin, is left behind. This may be purified by taking it up with a small amount of chloroform and reprecipitating with a mixture of sulphuric and petroleum ether.

Several workers have tried to find a relationship between the digitoxin content and the activity of the preparations, as determined by biological methods, but the results, in almost every case, have proved a failure, as will be seen by a study of the following tables, which we have brought together for the sake of comparison.

Ziegenbein^c conducted such a series of comparative experiments, estimating the toxic dose upon frogs, employing leaves obtained from various localities.

^a According to Kiliani, München. med. Wehnschr., 1907, LIV, 886, the widely advertised proprietary preparation digalen consists of a solution of impure digitalein.

^b Keller, Ber. d. deutsch. pharm. Gesellsch., Berl., 1897, VII, 125.

^c Ziegenbein, Arch. d. Pharm., 1902, CCXL, 454.

No.	Specimen.	Digitoxin content.	Toxic dose for 100 gram frog.
		<i>Per cent.</i>	<i>Gram.</i>
1	Leaves from North Harz, 1901.....	0.33	0.03
2	Leaves from North Harz, 1901 (selected).....	.163	.03
3	Leaves from South Harz, 1901.....	.14	.04
4	Leaves from South Harz, 1901 (selected).....	.185	.03
5	Leaves from North Harz, 1901.....	.125	.03
7	Leaves from Thuringia.....	.115	.05
10	Leaves, old, 1900.....	.226	.06
11	Leaves, Harz (finely powdered).....	.235	0.04-.05
12	Leaves, Harz (finely powdered).....	.18	.05

Famulener and Lyons^a carried out a similar research with the following results:

	Specimen fluid extract of digitalis.	Purified digitoxin content.	Toxic dose for 40 gram frog.
		<i>Per cent.</i>	<i>Gram.</i>
A.....		0.196	0.026
B.....		.258	.029
C.....		.182	.038

Barger and Shaw^b found that the ratio of toxicity of the tincture of digitalis to the toxicity of the digitoxin contained in the specimen varied in the series of nine tinctures from 3.5 : 1 to 6.9 : 1, or, in other words, tinctures from 3.5 to 6.9 times as toxic as the digitoxin which was obtained by chemical assay. Focke^c and Fromme carried out a similar set of comparative experiments and concluded that the digitoxin content and the physiological activity as determined by experiments on the frog did not run parallel. Reed^d and Vanderkleed, using guinea pigs, claimed to have found a certain parallelism, but a study of their results shows that the parallelism is by no means without exceptions:

No.	Preparation.	Chemical assay. Gram digitoxin in 100 cubic centimeters.	Physiological assay. M. L. D. ^e for guinea pig of 240 grams weight.
		<i>Grams.</i>	<i>c. c.</i>
1	United States Pharmacopœia tincture.....	0.0377	0.6
2do.....	.023	1.0-1.25
3do.....	.0277	.75
4do.....	.0254	1.0
5	Fat free tincture.....	.027	1.0-1.25
6	Fluid extract.....	.264	0.1
7do.....	.2405	.09
8do.....	.234	.1
9	Powdered extract.....	f1.061	.08
			g. 0.019-0.025

^a Famulener and Lyons, Proc. Am. Pharm. Ass., Phila., 1902, L, 415.

^b Barger and Shaw, Chem. and Physiol. Assay of Digitalis Tinctures, Handbook of Pharmacy, 1904, 541; Pharm. J. and Tr., 1904, LXXIII, 249.

^c Focke, Deutsch. Aerzt. Zeit., 1904, VI, 292.

^d Reed and Vanderkleed, Am. J. Pharm., Phila., 1908, LXXX, 110.

^e M. L. D.=minimum lethal dose.

f Per cent.

g Gram.

These figures certainly show a closer relationship than has been obtained by the previous workers.

Since we have then no satisfactory chemical method of estimating the activity of digitalis preparations, attention has been directed toward the development of assay by physiological methods. Several have been employed in the past ten years and the results obtained by their aid have served to emphasize the necessity of some way of standardizing these drugs. In both this country and in Europe many writers have demonstrated by these physiological tests the great variability of strength which exists not only in the galenical preparations of the drug but also in the so-called pure preparations themselves.

Among these investigators may be mentioned Bennefeld, who in 1881 showed that for rabbits the lethal doses of eight digitalis tinctures varied about fourfold.

Bührer (1900) demonstrated on frogs that some of the fluid extracts of digitalis were four times as strong as others.

In 1902 Fränkel showed that six infusions of digitalis varied from 100 to 275 per cent, and six tinctures from 100 to 400 per cent.

Siebert (1903) found in fifty experiments on digitalis leaves that the fatal doses per 100 gram frogs varied from 0.03 to 0.075 gram.

Edmunds in 1907 showed that seventeen tinctures of digitalis purchased in the open market varied in strength as 1 to 4, while Gottlieb (1908) found the same ratio to exist in Heidelberg. Reed and Vanderkleed (1908) found the toxic dose for guinea pigs of 240 grams weight varied in four tinctures from 0.6 to 1.25 c. c.

These variations in strength depend upon several factors, among which may be mentioned the source of the plant; for example, Ott^a has pointed out that Bohemian leaves are more toxic than others. At the present time the English leaves are considered the best. The plants growing wild are preferred to the cultivated variety, and those growing in sunny places to those in the shade, and those grown in dry seasons to those gathered in rainy. However, the most important factor in determining the activity of the leaves is the manner of drying and the mode of preservation, the influence of which has been especially studied by Focke (p. 24).

The experiments of Bennefeld and others to determine the relative activities of different members of the group were carried out along essentially the same lines and embody the same principles as are employed to-day in the biological standardization of these drugs. It was but a step from one to the other; the first writers determined the relative activity, while the later writers merely corrected these variations by such means as concentration or dilution of the preparations. To get then any comprehensive idea of the development of modern physiological standardization it is necessary to go further back than

^a Ott, Verhandl. d. Cong. f. innere Med., Wiesb., 1901, 89.

the first paper strictly devoted to the standardization problem and examine the earlier methods in vogue. We have therefore given short abstracts from earlier writings of such articles as bear upon the subjects before considering it in the light of more recent works, not only digitalis being discussed, but some other drugs belonging to the same group, such as *strophanthus*, as the same methods apply to all the members of the series.

In 1865 Fagge and Stevenson, in an address before the Royal Society, claimed that physiological tests would be of great medico-legal importance.^a They had studied digitalin especially and said for this purpose frogs were better adapted than the higher animals, as the various organs could be examined, the animals exhibited no fear, and the drugs acted quickly upon them.

In their paper published in 1866 they made a report upon the relative activity of several members of the digitalis group, among them being "antiar," *helleborus viridis*, squills, digitalin, and the infusion of digitalis. The method employed was to weigh the frog, attach it to a piece of cork, and expose the heart, avoiding hemorrhage as far as possible. It was then injected beneath the skin of the thighs and flanks and the time noted at which systolic standstill of the ventricle occurred. The length of time between the injection of the drug and the stoppage of the heart determined the relative toxicity of the different drugs. Fagge and Stevenson considered that the season of the year did not alter the reaction of the frogs to the drugs.

Ten years later Koppe^b published the results of his investigations upon the relative toxicity of the active constituents of digitalis, digitoxin, digitalin, and digitalein. His experiments were carried out upon frogs, cats, dogs, and rabbits. In his work on frogs he employed both *Rana temporaria* and *R. esculenta* and showed how much more susceptible the former were than the latter. His method was to expose the heart in the usual manner and inject the drugs, noting the time when systolic standstill of the heart appeared.

The dogs were either injected subcutaneously or the drug was administered by the mouth, changes in the rate of the heart and the strength of the beat being noticed, as well as the time when nausea and vomiting occurred. To cats the drug was administered both subcutaneously and by the mouth and the amount necessary to produce vomiting noted. Large doses produced alterations in the pulse rate. The drugs were given subcutaneously to rabbits and produced in them as the most prominent symptom a more or less complete paralysis associated with irregularity and slowing of the heart rate.

^a C. Hilton Fagge and Thomas Stevenson, Application of physiological tests for certain organic poisons, and especially digitaline. Reprinted from *Guy's Hosp. Reports*, 1866.

^b Koppe, *Arch. f. exper. Path. u. Pharmacol.*, Leipz., 1875, III, 274.

Fr. Bennefeld^a in 1881 undertook an investigation of the relative activity of tinctures of digitalis obtained from different parts of Germany. He first tried to compare them by means of their specific gravities and the amount of the dried residue, but his results, confirming those of Schneider,^b showed that such examinations were worthless. He then adopted the physiological method, employing rabbits as experimental animals.

The tinctures were prepared for examination by evaporating 25 c. c. and drying the resulting residue to constant weight over sulphuric acid. The residue was digested on a water bath for fifteen minutes at a moderate temperature with 15 c. c. of distilled water, was then filtered as quickly as possible and brought to a volume of 20 c. c. Before injection it was heated to body temperature.

The rabbits used were of the same age, weight, and resistance as far as possible. After inserting a cannula into a jugular vein, the modified tincture was injected at regular intervals in 0.5 c. c. doses until the animal died or the 20 c. c. was exhausted.

His results showed that the minimum lethal dose for the eight tinctures varied from 3.36 to 15.97 c. c. of the residue solution per kilogram, body weight, while the time of death varied from eleven to fifty-four minutes.

Frankel^c adopted still another method to determine the comparative activity of different preparations of digitalis. Dogs weighing between 10 and 18 kilograms were curarized and the drug injected subcutaneously in doses not exceeding 10 c. c. His standard for comparison consisted in the amount which was necessary to produce the digitalis effect, viz, a decrease in the rate of the heart with an increase in the volume of the single beats. He also registered the blood pressure.

He found marked differences between the various preparations in the amount necessary to bring about the desired effects, which he thought might be partly due to individual variations in the dogs and also possibly to the curara. The tincture was found to be very weak, while the acetum was the stronger preparation, but the active amounts of both acetum and infusion were quite variable.

Laborde and Duquesnel^d examined two samples of digitalien (Nativelle) as to their chemical purity and physiological activity, using for the latter purpose frogs and guinea pigs.

The hearts of the frogs were exposed and the drugs injected in 5-milligram doses, the effects being noted. With one preparation

^a Fr. Bennefeld, *Über Digitalis-Tincturen, Comparativ-experimentelle Untersuchungen*, Inaug. Dissert., Göttingen, 1881.

^b von Schneider, *Arch. d. Pharm.*, 1879, CCXV, 412.

^c Frankel, *Charité-Ann.*, Berl., 1881, VI, 207.

^d Laborde and Duquesnel, *Comp. rend. hebd. des Séances et Mém. de la Soc. de Biol.*, 1884, XXXVI, 93.

the heart stopped in systole in two minutes, while with the second sample it continued to beat for hours. The difference in physiological activity was also shown by means of graphic records.

The results obtained on the frogs were confirmed by the injection of 5 milligrams of each sample into two guinea pigs, the length of time till death occurred serving as a means of comparison.

Similar methods of comparison were also employed by Laborde^a in his study of the purity and activity of the digitalines in use at the hospitals of Paris.

Gley^b compared the toxicity of ouabaine and strophanthin by means of experiments upon several varieties of animals. Upon frogs he showed that with equal doses of the two drugs ouabaine would stop the heart in half the time that strophanthin would. He then compared the toxic dose of the two drugs upon guinea pigs, dogs, and rabbits; in the latter case injecting the drugs into the vein of the ear, in the other cases using subcutaneous injection.

Reusing^c carried out a series of experiments comparing the actions of strophanthin and digitalis upon the frog's heart, employing two methods in his work. In the first he studied the effect directly upon the exposed heart, the pericardium not being opened. In the second method the Ludwig-Coat's heart apparatus was employed, the perfusion fluid to which the drugs were added consisting of two parts of 0.65 per cent NaCl solution with 1 part of defibrinated hog blood.

Bardet^d undertook in the same year an examination of the relative activity of the various active principles of digitalis and employed the simplest method which is in use to-day to standardize these drugs, viz, that of determining the lethal dose for animals, using frogs and rabbits.

An examination of a number of the so-called digitalines of commerce was made by Fouquet,^e who ascertained the toxic dose of the different samples when they were injected hypodermically into frogs, rabbits, and dogs. In this way he studied the relative activity of crystallized and amorphous digitalin, digitoxin, and digitalein.

In 1893 Prevost^f examined a number of the preparations which had been included in the Swiss Pharmacopœia III, among them being some members of the digitalis group. His experiments were carried out upon frogs (mainly *R. temporaria*), upon which he sought the minimal dose of the drug which would produce definite stoppage of

^a Laborde, *Comp. rend. hebdomadaire des Séances de l'Académie des Sciences et Médecine de Paris*, 1884, XXXVI, 599.

^b Gley, *Comp. rend. des Séances de l'Académie des Sciences*, 1888, CVII, 348.

^c Reusing, *Über die Einwirkung des Strophanthin auf das Froschherz*, Inaug. Dissert., Würzburg, 1889.

^d Bardet, *Bull. et Mém. Soc. de thérap.*, Par., 1889, 2d ser., XVI, 253.

^e Fouquet, *Bull. gén. de thérap.*, 1892, CXXII, 71.

^f Prevost, *Rev. Méd. de la Suisse Rom.*, Genève., 1893, XIII, 505.

the heart and death of the animal. He considered the frog as the most suitable animal upon which to test the relative activity of the members of this group as mammals vary considerably in their susceptibility to them. In his earlier experiments he did not weigh the animals, but later adopted this precaution, regarding the weight as being a factor of some importance, but at the same time not considering that the action of the drug upon different frogs is in any absolute relation to their weights. The frogs he employed were an average size, being between 25 and 30 grams. He confirmed some of the results obtained on frogs by experiments upon guinea pigs, the comparative results being as follows:

Animal used.	Toxic dose.		
	Fluid extract con-vallaria.	Fluid extract digitalis.	
		No. 26.	No. 6.
R. temporaria, average size.....	c. c. 0.003	c. c. 0.02	c. c. 0.04
Guinea pig, per 100 grams.....	.006	.01	.02

It will be seen that the two digitalis preparations show exactly the same ratio on both animals.

In 1895 Prevost ^a repeated his experiments upon these preparations to see if they had deteriorated in the intervening time. In this case he used *R. esculenta*, realizing, however, that they did not offer the same susceptibility as *R. temporaria*.

Mlle. M. Piotrowska ^b studied the comparative toxicity of a number of the members of this group and the effect upon their toxicity of the mode of administration, whether subcutaneously or by the mouth. For this purpose she used frogs (*R. temporaria*) almost exclusively, determining the toxic dose and comparing them on a basis of 100 grams body weight. Some of her results she confirmed by determining the toxic dose for cats and rabbits, comparing them on the basis of kilograms of body weight.

The examination of the plant dialysates was made the subject of investigations by several workers, one of the earliest being Jacquet.^c These dialysates were prepared by Golaz of Vevey, Switzerland, from fresh plants and made of such strength that 1 part of dialysate corresponded to 1 part of leaves. By using great care in the collection of the leaves, gathering them in the same region during sunny weather, using them fresh, and making the product up to a uniform volume, it was believed that a definite dosage of digitalis was attained, as

^a Prevost, Rev. méd. de la Suisse Rom., Genève., 1895, XV, 453.

^b M. Piotrowska, Inaug. Dissert., Geneva, 1896.

^c A. Jacquet, Cor.-Bl. f. schweizer Aerzte, 1897, XXVII, 326.

so many of the disturbing factors had been eliminated. It was naturally impossible to make allowances for the yearly variation which was known to take place, and therefore the argument for a uniform product based upon these facts alone falls to the ground. Jacquet, who pointed out in his paper these advantages of the dialysates, made a number of physiological tests on the dialysates of *digitalis* and *Adonis vernalis*. He employed frogs (*R. esculenta* and *temporaria*) with exposed hearts, injecting the drug into the lymph sacs and noting the length of time before death. He also studied their action upon the blood pressure and heart rate in rabbits and noted the toxic dose.

By a comparison of the results obtained in this way with those he obtained under similar conditions using digitoxin and digitalium verum he estimated the dose of the dialysates which it would be proper to employ in man, it being possible to do this as the therapeutic dose of the active principles for man was already known.

It appears that Jacquet approached more nearly to physiological standardization than any of his predecessors, as he points out the advantage of the dialysates in affording an exact dosage, but it was not until his second paper,^a which appeared in December, 1898, that he seems really to have adopted physiological standardization. As stated above, he believed that a uniform preparation had been obtained by eliminating so many factors which go to make the great variations which are found in the ordinary galenical preparations; but as he stated then, he was unable to avoid the yearly variation in plants. This was evidently quite a large factor, as, examining the 1896 specimen, he was able to isolate 0.16 per cent of the active constituent, while in the 1897 preparation there was only 0.096 per cent. This variation he ascribed to the fact that the weather was unsettled at the time of gathering the leaves, and on that account the plants contained an unusually large amount of water. He therefore compared the two dialysates by physiological methods and found the same relative differences, for while ten drops of the 1896 specimen produced systolic standstill in frogs, it took twenty drops of the 1897 preparation. Likewise, it took double the amount of the 1897 preparation to kill rabbits.

Recognizing at this time the yearly variation, which is apparently of a good deal of importance, he suggested that either a yearly change of dose would be necessary or an adjustment of the solution by evaporation or dilution as might be necessary, so as to give a uniform product. The latter course he thought preferable. This paper, in which he really adopted the physiological method of standardization, was, however, preceded by one by Houghton which appeared in America in October, 1898.

^a A. Jacquet, Cor.-Bl. f. schweizer Aerzte, 1898, XXVIII, 745.

No reference is directly made in Jacquet's paper as to the effect of the weight of the frogs upon the results, except, in the protocols, the size is noted as "large" or "medium."

In his experiments upon rabbits he used two methods. Upon most he measured the effect upon the blood pressure and heart rate when the drug was injected into the jugular vein and calculated also the toxic dose per kilogram body weight. In other cases he injected the drug subcutaneously.

It appears strange that, although so much work had been done on the comparison of the relative strengths of the different members of the digitalis group, no practical application was made of the methods developed until more than thirty years after Fagge and Stevenson published their results. As pointed out, it was not until 1898 that the application of these physiological tests was advised for the production of uniform pharmaceutical preparations. In that year Houghton^a published his method for the physiological assay of strophanthus, basing it upon the fact that the killing power of the cardiac drugs for frogs of definite size and species, kept under proper conditions, is constant per gram of body weight. He had tried rabbits, guinea pigs, and rats, as well as frogs, but came back to the latter as being most satisfactory as he found too great variation in the blood pressure of dogs and rabbits under the action of digitalis to allow of this method being of use. Any species of frogs may be employed, provided both the standard solution and the unknown preparation are tested upon the same species, for, while animals of different species vary in their reaction, those belonging to the same are much alike. Also frogs of any weight may be used, providing the proper allowance is made for the variation, but in testing a preparation, it is best to use frogs of nearly uniform size, varying from one another not more than 3 grams. The frogs to be employed should be freshly caught and carefully handled, being kept in wet moss until they can be placed in suitable pools at the laboratory.

The dose of the drug to be tested is calculated according to the weights of the frogs to be employed and made up with salt solution so that it will measure about one-half cubic centimeter, and is then introduced into the abdominal lymph sac by means of a pipette. The frogs are placed in separate jars and allowed to remain for twelve hours, at the expiration of which time they are examined and note made as to the dead and living animals. By a preliminary test in which the limits of dosage are quite wide some idea is formed as to the strength of the preparation and a second series of frogs is injected, still further narrowing the dose. When by this second group the probable toxic dose is obtained, a new series of five frogs is injected, and if the dose is correct at least three frogs out of the five should be

^a Houghton, J. Am. M. Ass., Chicago, 1898, XXXI, 959.

killed. By a simple calculation the relative strengths of the unknown and the standard preparation can then be obtained.

An important contribution to the subject of biological assay was furnished by Carl Bühler,^a who investigated the activity of some of the toxic fluid extracts, among them being digitalis and convallaria. He selected frogs and rabbits as experimental subjects. The frogs, either *R. esculenta* or *temporaria*, were chosen with great care and obtained fresh every two weeks, but he used only one species for one preparation and for digitalis only *R. temporaria*. He seems to be the first to note any effect of sex upon the results and says he finally employed females exclusively. The effect of season upon the reaction of the frogs was corrected by repeating his experiments at various times of the year. Bühler seems not to have considered the size of the animal as being important, for while he weighed the frogs before the drug was injected, the weight was not used in calculating the dose or judging the results. The method he used was as follows: The frog was stretched out on its back and then, with as little hemorrhage and other injury as possible, its heart was exposed. The rate was counted at once and again after five minutes when the drug was injected into the thigh lymph sac and the animal put into a moist chamber and observed at intervals. The dose of the drug to be tested was prepared by diluting the fluid extract with different amounts of salt solution and injecting one-half cubic centimeter. The end reaction or standard consisted in finding the smallest amount of drug which would cause systolic stoppage of the heart within twenty-four hours. The comparative strengths of the different specimens were then reckoned as so many milligrams, according to the dilution of the drug, without paying any attention to the weight of the animal. By this method he found the specimens of 1897 varied in the ratio of 1 to 4, while the 1898 fluid extracts were weaker, but more uniform in strength. He thought it was possible that this apparent weakness was due to a difference in the reaction of the frogs, as the 1898 specimens were examined one and one-half months after those of 1897, and he had found that even in from two to four weeks the animals might alter very considerably in their reaction to one and the same drug. This variation he thought was due to their winter fast, but in this case his supposition was proved incorrect by subsequent examination made in December, 1899.

Bühler further continued his experiments, employing rabbits which were arranged for blood pressure estimations. The diluted drug was injected intravenously at intervals of from five to ten minutes, until the lethal dose was reached. By carrying out several experiments

^a Bühler, Untersuchungen über die Wirksamkeit einiger toxischer Fluid-Extracte, Inaug. Dissert., Basel, 1900.

an average lethal dose was obtained, which was based upon the toxic amount per kilogram body weight.

The variations obtained on rabbits did not appear as great as with the frogs, being only 200 instead of 400 per cent. He tabulates his results as follows:

Fluid extract digitalis.	1897.		1898.	
	Frogs.	Rabbits.	Frogs.	Rabbits.
	Mg.	Mg.	Mg.	Mg.
A.....	17	400	33	590
C.....	25	630	25	780
D.....	33	770	25	740
F.....	67	800		

The relation between the different preparations is not the same with the frogs as it is with the rabbits, and Bühner had expected this discrepancy, as he said the two animals are so entirely different. However, fluid extract A is shown to be the strongest by both methods.

Fränkel^a assayed Merck's digitoxin and later took up different infusions of digitalis which he obtained in and around Heidelberg. His method was to ascertain the amount of drug which would produce systolic standstill of the frog's heart in about an hour's time. If the heart stopped in a shorter time than fifty minutes the dose was lessened, while if it had not ceased to beat in one hour and ten minutes the dose was increased. The frogs (species not mentioned) were injected in a lymph sac, the amount of fluid being usually 1 c. c. except in some cases 2 or even 3 c. c. were employed. The animals were weighed and the toxic dose per 100 grams body weight calculated by a simple ratio.

His results showed that six infusions varied in toxic dose from 2.5 to 6.9 c. c., a difference of 100 to 275 per cent. Six tinctures examined varied from 0.6 to 2.5 c. c., 100 to 400 per cent, and seven strophanthus tinctures varied from 0.015 to 1.0 c. c. Fränkel thinks we are justified in transferring these results to the higher animals as Bühner was able to show a parallelism between the action on rabbits and on frogs, while he himself with four digitalis preparations showed the same ratio to exist on cats as on frogs. (Bühner's table, as he himself pointed out, shows a certain parallelism, but by no means an exact one.)

In 1902 Famulener and Lyons^b undertook a study of the relative strength of various preparations of digitalis and related drugs. They employed frogs (species not mentioned), choosing those of about 40 grams weight and injecting the preparations to be tested into the ventral lymph sac by means of finely pointed pipettes. At the

^a Fränkel, *Therap. d. Gegenw.*, Berlin u. Wien, 1902, XLIII, 106.

^b Famulener and Lyons, *Proc. Am. Pharm. Ass.*, Phila., 1902, L, 415.

end of an hour the heart of the animal was exposed and examined. If the heart was found completely paralyzed the dose was too large; if pulsation still continued the amount was too small. The correct "end reaction" adopted by the writers was "paralysis" of the apex of the ventricle, but at the base of the ventricle there should occasionally be a faint wave of contraction while the auricle, though much distended, would continue to pulsate regularly. When the correct dose was found the amount necessary to kill a frog of standard weight (40 grams) was calculated by a simple proportion.

Famulener and Lyons found the reaction of the frogs very uniform, for not more than one or two out of a dozen healthy frogs showed a variation in susceptibility of as much as 10 per cent. To avoid this source of error, when they had determined the minimum dose in the manner indicated, they took a further series of three frogs, injecting into one the minimum dose, into a second a dose 10 per cent above the minimum, and into the third a dose 10 per cent below it. If any of this latter series showed irregularities further corrections were made. More uniform results were obtained by this method than could be obtained in the assay of such drugs as opium and nuxvomica by chemical means. The authors give a table showing the results of their examination into the activity of the pure principles of digitalis and related drugs as well as of the galenical preparations. A very important contribution in their paper is a comparative study of the digitoxin content of three preparations of digitalis fluid extract with their activity as determined by physiological methods. This was referred to earlier in our article (p. 9).

Wolff^a made a short report upon the biological dosage of digitalis preparations commenting upon the findings of Fränkel and quoting Professors Kobert and Gottlieb upon the necessity for a government station for the standardization of digitalis preparations. He then describes the method adopted by Brunnengräber, of Rostock, to bring into the market uniform preparations of these drugs. The leaves are collected on sunny days from wild plants before they begin to flower, carefully sorted to free them from any foreign leaves, and are then dried quickly in a vacuum at a definite temperature. In this way the fermentation which the leaves usually undergo during slow drying is avoided. Tinctures prepared from leaves, dried in this way, were examined by Professor Kobert, who reported them free from harmful split products and high in content of active principles. Strophanthus tinctures were also prepared from the fresh green seeds of *S. Kombé* which had not been freed from fat and these too were very active. An infusion made from 5 milligrams of digitalis leaves produced systolic standstill of the frog's heart as did also 0.02 c. c. of the tincture of strophanthus.

^a Wolff, Therap. d. Gegenw., Berlin u. Wien, 1902, XLIII, 423.

Ziegenbein^a during 1901 and 1902 examined a number of specimens of digitalis leaves obtained from different localities estimating the digitoxin content and conducting comparative experiments by physiological methods. His results as given in the table on page 9 show that no definite parallelism between the two can be found. The toxicity of the digitoxin, which he was able to isolate by the Keller or Keller-Fromme method, only accounted for about one-third of the activity of the leaves from which it was obtained. He examined the toxicity of the extract which was left after shaking it out with chloroform to remove the digitoxin, and found that some principles which were insoluble in chloroform still remained and accounted for another one-third of the activity of the leaves, but the remaining one-third could not be accounted for. He carried out some experiments to determine the effect of the fineness of the drug upon the toxicity of the infusion which when powdered gave a higher value than did infusions made from leaves which were simply cut up. The toxic dose for the former was found to be 0.048 gram, while the latter required 0.064 gram to produce the same effect, and when finely powdered the leaves were most potent requiring only 0.03 gram, the difference probably being due to the greater surface of the drug exposed to the solvent. The method he employed for the physiological estimations was that originated by Hans and Arthur Meyer. In this method, freshly caught male frogs (*R. temporaria*) were secured upon a board and the heart exposed in the usual manner. Definite amounts of the drug to be tested were then injected into the thigh lymph sac and the smallest amount was sought which would produce systolic standstill within two hours. The minimum lethal doses thus found were calculated upon the basis of 100 grams frog weight in order to allow of comparisons. Frogs weighing about 25 grams were chosen for the experiments, but Ziegenbein did not think that a few grams difference in weight influences the results to any appreciable extent. He was also of the opinion that the season of the year makes very little difference in the susceptibility of frogs.

In the following year Moschkowitsch^b published a critical study of the method of standardizing digitalis preparations by means of their action on frogs. His experiments were carried out on *R. temporaria*, which were fastened to a board and the sternum removed to permit of free observation of the heart, the pericardium being left intact to prevent drying. The drug to be tested was introduced into a lymph sac and its activity was measured by the time when it first produced an effect on the heart and by the time necessary to cause systolic stoppage.

^a Ziegenbein, Arch. d. Pharmacie, 1902, CCXL, 454. Ber. d. Deut. Pharm. Gesells., 1902, XII, 335.

^b H. F. Moschkowitsch, Arch. d. Pharm., 1903, CCXLI, 358.

The author studied pure principles and also galenical preparations, and the most important fact which he brought out and especially emphasized in his work was the great variability in the reaction of frogs. The time of the first appearance of the action varied between two and six minutes, but a still greater variability was shown in the time of the appearance of systolic standstill. He said he was greatly discouraged by the great capriciousness in the reaction of the frogs, and the hope of an exact estimation by physiological methods received a mighty blow.

While in the estimation of his dosage he did not usually take into consideration the weight of the animal, yet in discussing his results he had several opportunities to compare the action of the drug upon animals of the same size. In some of his tables this factor seems to be important, while in others it would appear that it could be ignored; the hearts of frogs of the same size given the same dose stopping in widely different times, while those of different sizes stopped after like intervals when given the same sized dose. His conclusion upon this phase of the question was that it was best to take into consideration the weights of the frogs in making an assay. Upon the important question as to the effect of the season upon the susceptibility of frogs he found that summer (July) frogs possessed far greater resistance than winter frogs.

He points out that his results do not confirm those of the earlier workers, but he thinks the individuality of the animal is an important factor. According to this author, unless animals of about the same weight and of the same species can be obtained from a certain section of the country at the same time of year greater reliance can be placed upon chemical analysis. At any rate, he concluded that it was only in a very general way that we could tell from physiological experiments as to whether a preparation was good or bad, and while the method was not necessarily useless it was defective.

In the same year Brondgrest^a also conducted a series of experiments to compare the action of the dialysate of *digitalis grandiflora* with *digitalinum purum* and the infusion of *digitalis purpurea*. He employed for this purpose the frog's heart in situ, using the suspension method combined with the Williams perfusion apparatus. He concluded that the dialysate of *digitalis grandiflora* acts the same as *D. purpurea* and as *digitalinum*.

Among the numerous writers upon the subject of standardization no one has contributed more than Focke,^b who published several articles between 1902 and 1906. His method has undergone one or

^a Brondgrest, Zentrbl. f. innere Med., Leipz., 1903, No. 24, 906.

^b Focke, Therap. d. Gegenw., Berlin u. Wien, 1902, XLV, 44; Arch. f. Pharm., 1903, CCXLI, 128, 669; Deutsche Aerzte Ztg., Berlin, 1904, VI, 272, 292; Therap. d. Gegenw., Berlin u. Wien, 1904, XLV, 250; Berlin klin. Wehnschr., 1906, XLIII, 642.

two important modifications since it was originally published, but otherwise it is essentially the same. He employs frogs (*Rana temporaria*) which are collected not earlier than the end of June. They are kept in a cellar in a box the bottom of which is covered with water, the latter being changed at least daily. The frogs should not be used before the third day of captivity and should be brought to the examining room six hours before they are needed, being placed in jars at a temperature not over 17°C . The examinations should be carried out in July, August, and September, during which months the susceptibility of the frogs does not differ greatly, and also during this time no distinction need be made with reference to sex. Animals weighing between 25 and 30 grams are selected and fastened to a board in the usual manner, and the heart is exposed without allowing bleeding or other injury (pithing is not permitted at this time). After opening the pericardium a slight pressure upon the abdomen will cause the heart to protrude from the opening, where it will remain in plain view. A measured quantity of the infusion to be tested is now injected into the two leg lymph sacs, about 0.3 c. c. into each or 0.6 c. c. in all. Both lymph sacs are used so that the distended skin will not force the drug out of the opening by pressing upon a large bulk of fluid. Systolic standstill of the heart is now watched for and it should appear in ten or fifteen minutes. When this is observed and the time noted, the frog is pithed and weighed.

Two more frogs are now selected of about the same weight, and the dose to be injected is determined by the effect of the primary dose. If the heart, in the first frog, stopped in less than ten minutes, a relatively smaller dose is used, while if it did not stop in twenty minutes a larger dose should be employed. A sufficient number of frogs should be used so that four are found in which the hearts have stopped between seven and twenty minutes. The toxic value (V) of the drug is then determined in relation to the size of the frog (P) divided by the dose of the drug given (d) multiplied by the time it takes for the heart to come to a systolic standstill (t): $(V) = \frac{P}{d \times t}$. The " V_s ,"

having been determined for each trial, are averaged and the amount found is considered as representing the value of the preparation of digitalis which has been tested. Focke considers that a good specimen of leaves should give a standard value of 5. He originally accepted all readings between ten and twenty-five minutes, but the method was modified later to time limits of seven to twenty minutes, as he found the results were much more uniform. If the heart stops in a shorter time than seven minutes, the differences in the values found are greater, or if over twenty minutes, he found the readings were much more variable, and the " V_s " obtained were very small. For this reason he dislikes Ziegenbein's and Frankel's methods, the former

taking the least amount which will stop the heart which will usually occur anywhere between thirty-five and one hundred minutes (Ziegenbein says within two hours), while the latter takes as his end reaction the stoppage in from fifty to seventy minutes. Focke, therefore, prefers his method because it is more convenient, taking less time and because it is more exact, showing according to him only 8 per cent of error.

After Focke developed this method he considered a number of factors which influence the results of standardization and the variability of digitalis preparations. In order to determine the effect of season upon the frog's susceptibility, he examined leaves which had been very carefully dried and which would retain the same value at the various times of the year. He found that in the spring they gave an average value of 2.66; from the end of June to October, 4.36; and in October, 5. At this time he considered these variations due to differences in the nutrition of the frogs, but later researches^a seemed to indicate that the temperature factor might also play some part in changing the V obtained.

Thus frogs operated on at a temperature of 17.5° to 18.5° in December showed a V of 5.5. At the same temperature the same drug had a V of only 4.7 the last of February, but at 19° to 21° gave nearly the original value. In June, to obtain this value, it was necessary to increase the temperature to from 22° to 23°, at 18.5°, the original December temperature, the value being only 3.8. At the same temperatures there seemed to be no difference in the reaction of frogs which had been captured recently and those kept in captivity for several months.

Physiological standardization may be carried out according to Focke, therefore, at any time during the year, but it is first necessary to standardize the animal against digitalis leaves of known value by regulating the temperature and then by cooling or heating the operating room to carry out the assay at the temperature found to show the standard value as arbitrarily adopted.

It has been recognized that wild plants are more toxic than cultivated, and in confirmation of this view Focke found the former to give a V of from 5 to 6, while the latter gave as Vs 2.6 and 3. The yearly variation in plants from the same district he found to be quite marked, the weakest giving a value of 4.3, while the strongest had a V of 8.5. It has been universally recognized also that the second-year plants just before flowering are more active than the first year. In agreement with this view Focke found that the second-year leaves collected in June have a toxic value 15 to 20 per cent higher than first-year leaves collected from plants grown in the same locality. Plants flowering in July seed in August, and at this

^a Focke, Arch. d. Pharm., 1907, CCXLV, 646.

time the leaves show the effect by a lessened toxicity, the relation being reversed, as at this time the first-year leaves are stronger. The effect of daylight was found to be very slight, even if the leaves were exposed to its influence for a year. As to the effect of the aging of the leaves he found that if they were collected and dried in the air in the ordinary way and preserved in nonair tight flasks they will lose a large part of their activity.

The greatest factor in this deterioration Focke considers to be the moisture content, and the changes which the leaves undergo during the first few months after their collection are largely due to this, as in the presence of moisture certain ferments present in the leaves are able to destroy some of the active constituents. To avoid this, he heats the leaves rapidly and strongly at a temperature not over 100°C ., and when they are dried so as to contain only about $1\frac{1}{2}$ per cent moisture they are preserved in lots of 50 grams in dark, airtight jars. He found that if dried and preserved in this manner they lost only 5 per cent in V in a year. The last 1 per cent of moisture left in the leaves seemed to be bound in some manner, so that it was not active.^a To show the importance of the moisture content factor, Focke believed that only about one-fifth of the differences in strength were due to all the other factors.

To avoid the variation due to the different localities, the leaves from all the different sources should be powdered after drying and mixed, so as to give a uniform product.

Siebert^b reports the efforts of himself and Ziegenbein to determine a method by which digitalis and strophanthus preparations could be standardized biologically. The method adopted by them was the one developed by Arthur and Hans Meyer, which has been described earlier in the discussion of Ziegenbein's work.

In fifty experiments with digitalis leaves the most active preparation showed a toxicity of 0.03 gram for 100 grams frog weight, while the weakest required 0.075 gram to produce death. They, therefore, adopted as a standard strength for digitalis leaves 0.04 gram for 100 grams frogs.

The variation in strophanthus preparations was as follows: Weakest 0.06, strongest 0.008 c.c. for 100 grams frogs. The standard they adopted was 0.02 c.c.

An important chapter on the subject relating to the comparative study of the chemical and biological methods of assay of digitalis

^a In this connection it is interesting to note that in 1867 Tourdes (*Gaz. med. de Strasb.*, 1867, XXVII, 191) pointed out that the reason the digitalis preparations obtained in Strassburg were superior to those used elsewhere was because the leaves of the second year's growth were employed after having been selected carefully and dried first in the shade, and then in an oven at a temperature not over 40°C . The leaves were then preserved in tin or glass vessels away from the light and moisture.

^b Siebert, *Berl. klin. Wchnschr.*, 1903, XL, 813.

was contributed by Barger and Shaw^a in 1904. Their investigations were carried out upon tinctures of digitalis prepared according to the British Pharmacopœia and obtained from various commercial sources. For the estimation of the digitoxin content they used Keller's method with slight modifications. For the biological experiments male frogs (*Rana temporaria*), weighing between 20 and 35 grams, were used almost exclusively, but comparative experiments were limited to those of nearly the same weight. The experiments were carried out in the early summer.

The tinctures were modified by evaporating a known amount over a hot-water bath and suspending the residue in hot water. The digitoxin employed in some of these experiments was dissolved in alcohol and later diluted with water so as to give it an alcoholic strength of 10 per cent, the digitoxin being injected in suspension. In all cases the drugs were injected into the dorsal lymph sac, the volume for decisive experiments being 1 c.c. The animals after injection were kept in a moist atmosphere and the time noted when the heart stopped, which always occurred within three hours, if at all.

After an estimation by chemical means of the digitoxin content in nine tinctures, they estimated the toxic value of the same tincture by the biological method described. The results obtained by the latter method show less variation between the tinctures than is usually found, as the strongest was only one and one-half times as toxic as the weakest.

They show that, on account of the slight toxic strength of digitalin and digitalein, a supposition exists that the toxicity of a tincture runs parallel to the digitoxin content (by Keller's method), but this is not correct, as they found that the ratio of toxicity of tinctures to the toxicity of the digitoxin content in them was as 1 to 3.5, 5, 3.7, 5.5, 6.9, 4.1, 4.1, 5, and 4.2.

The writers then estimated physiologically the toxicity of the water soluble active constituents, and this, added to the toxicity of the digitoxin, was compared to the total toxicity of the tincture. The results show that about 50 per cent of the tincture toxicity was still unaccounted for even when both water-soluble and insoluble constituents were considered.

In order to find the cause of this discrepancy they prepared a tincture from chaff and hay and added to this 0.04 per cent crystallized digitoxin. By biological methods 0.0375 per cent was demonstrated, while by Keller's method only 0.01 per cent was found. The cause of the difficulty was shown by further experiments to depend upon the fact that much of the digitoxin adheres to the resin which separates out when the alcohol is evaporated off from the tincture, this being lost in the chemical method of estimation, but appearing in the physiological.

^a Barger and Shaw, Pharm. J. & Tr., London, 1904, XIX, 249.

According to their results it appeared that 1 gram of the tincture would kill a 59-gram frog, but the water soluble active constituents would only kill a 15-gram frog. The 44 grams difference in frog weight therefore ought to be killed by the insoluble portion or digitoxin. The toxic value for the digitoxin for only a 17-gram frog had been demonstrated by the Keller method, however, leaving 27 grams of the toxicity of the digitoxin of the original tincture still unaccounted for and which probably remains in the resinous portion when Keller's method of determination is used. In other words, only about one-third to one-half of the digitoxin present is isolated by this method, and the authors conclude, therefore, that the only reliable method for the assay of digitalis tinctures is the physiological one.

Freund^a studied the action of abyssinin and compared it with drugs of the digitalis groups, notably, digitalin, digitalein, digalen, the dialysate of digitalis, and strophanthin.

For the purposes of this investigation he used frogs and rabbits. With the former the heart was laid bare and attached to a suspension writing lever, thus obtaining tracings showing the progressive action of the drug. In some animals a solution of the drug was dropped directly on the heart, while in others it was injected into a lymph sac. In the case of rabbits Freund used the blood pressure changes as a method for comparing the relative action of the drugs.

In his study of the different heart drugs, Kakowski^b examined a number of digitalis preparations, among them being the infusion and the tincture. He employed the isolated hearts of frogs (*R. temporaria*), rabbits, cats, and dogs and showed that the infusion acted more strongly upon some of the animals than the tincture.

Still another modification of the use of a frog's heart in estimating the activity of members of the digitalis group was adopted by Santesson^c in his examination of the strength of different varieties of strophanthus seeds. In this method the drug was injected into a lymph sac of *Rana temporaria*. The animal was not tied down, but was held on its back in such a way that the contractions of the heart could be observed through the skin. In case it was necessary, a glass rod was passed into the esophagus so as to press the heart forward to facilitate the determination of its rate. Finally, to allow of exact timing of the appearance of the systolic standstill, the chest was opened and the organ observed directly. The standard dose employed by Santesson was that amount of the drug which would produce systolic standstill of the heart in thirty minutes, the dose being reckoned upon the basis of a 50-gram frog. Santesson's custom was to give a large dose at first, one that would be sure to kill, and on

^a Freund, *Zeitschr. Exp. Path. u. Therap.*, 1905, I, 557.

^b Kakowski, *Arch. Internat. de Pharmacod. Gand et Par.*, 1905, XV, 21.

^c Santesson, *Skandi. Arch. f. Phys.*, 1905, XVII, 389.

subsequent injections to diminish the amount until that dose was reached which would stop the heart in the required time. He points out that the biological standardization is not easy on account of the irregularity of the reaction of frogs. To avoid this as much as possible there should be taken into consideration the effect of season, species, body weight, temperature, condition of health, and, finally, a factor which can not be reckoned upon, viz, individual idiosyncrasy. The frogs employed by Santesson were captured in the autumn and kept in a cool place until they were used, in November and December. Males of about 50 grams weight were selected and kept in the examining room at least one hour before they were used. With these precautions Santesson showed that tinctures prepared from different varieties of *strophanthus* seeds varied in strength in the ratio of 1 to 4.

A second method of comparison was to perfuse the frog's heart, using William's apparatus, comparing the effect of the different drugs upon the pulse frequency, circulation rapidity (number of drops perfused per minute), and the pulse volume.

The results obtained by the two methods furnish a very interesting comparison.

Preparation.	Lethal dose for intact frog.	Lethal dose, isolated heart.
1.....	0.063	0.047
2.....	.10	.123
3.....	.22	.25
4.....	.10	.046
5.....	.064	.027
6.....	.051	.0925

Santesson calls attention to the fact that a certain parallelism exists in the results obtained by the two methods, but it is certainly very slight. He explains the lack of closer agreement as being due to the fact that the poison would not be so uniformly distributed in the fluids of the intact animal as in a fluid used to perfuse an isolated heart.

Dixon,^a in a paper on the biochemical standardization of drugs, considers the frog as the most suitable animal for digitalis standardization. In employing them the time of year should be taken into consideration, as they are most active and vigorous in the summer and least active in the spring, but their sensitiveness to digitalis will not vary over 50 per cent during the year. Those selected should be males of about 25 grams weight and free from abnormal conditions. The tincture, diluted with an equal amount of water, is injected into the dorsal lymph sac and 6 minims of this diluted tincture should

^a Dixon, Pharm. J. and Tr., London, 1905, p. 155; Manual of Pharmacology, 1906, p. 34.

produce systolic stoppage of the heart in one hour. Dixon proposes this as a standard "unit," and if a certain tincture does not correspond to this strength the pharmacist should make the necessary calculations, so as to give the patient a uniform product. The writer thinks the method proposed above may be accurately controlled by experiments upon rabbits.

In his *Manual of Pharmacology* (1906, p. 34), after discussing the frog method, Dixon says: "These drugs can be standardized more accurately by perfusing the isolated rabbit's heart with Ringer's solution and subsequently adding the drug." However, Sowton's results, referred to later, hardly confirm this statement.

Haynes^a sought to determine the relative activity upon the heart of the three important members of the digitalis group—digitalis, strophanthus, and squills—using tinctures which he prepared very carefully according to the *British Pharmacopœia*. He standardized these by determining the smallest dose of each which, when injected into the dorsal lymph sac of a frog, would cause systolic stoppage of the heart. He also carried out comparative tests upon rabbits with these preparations, injecting the drugs invariably into the stomach and watching for changes in the blood pressure as well as for the toxic effects upon the heart. In addition he studied their relative strength upon the excised hearts of rabbits, employing a modification of the Langendorff method and compared especially the effect upon the rate and the quality of the heart beat.

In respect to the suggestion that, on account of the variation in the strengths of galenical preparations of this series, the active principles should be substituted for them in general practice, Haynes says that in their isolation much of their potency is lost and that they require standardization even more than the galenicals.

The *Pharmacopœia* of Norway (1870) directed that official preparations of digitalis should be made from the plant growing wild in Norway. Wang^b undertook to determine whether the plants growing in that country offered any advantage as regards strength over those growing elsewhere.

He used frogs (*Rana temporaria*) and adopted Focke's method of assay described earlier. His experiments were carried out in Strassburg in October, 1905. The frogs were kept in a cool cellar, and the evening before they were needed they were placed in a cool room, being brought to ordinary room temperature two or three hours before they were used. The animals were injected with the 10 per cent infusion through the lateral lymph sacs into the two thigh lymph sacs. In this manner any escape of the drug was avoided when the chest was open. The heart was exposed as soon as the animal was

^a Haynes, *Bio-Chem. Jour.*, 1906, I, 63.

^b Wang, *Festschr. f. Olof Hammarsten*, 1906.

injected and the time noted when systolic standstill appeared. Wang, in common with some other workers, found it hard to decide at just what time this end reaction occurred, and he therefore used the stoppage of the circulation as an end reaction. His results, using Focke's formula to give the toxic worth of the leaves, are very variable. In some of the tables, especially Table I, in which, in sixteen estimations of one preparation, he obtained values between 3.6 and 8.8, with an average of 5.2. The other tables are not nearly so irregular in their results, since in these he calculated his dose according to the body weight of the animal employed. Table III, for instance, only shows slight variations from 4.7 to 5.7, with an average worth for the specimen of 5.3.

Löwy^a carried out experiments with infusions of digitalis to determine the effect of hydrochloric acid and pepsin, in the per cents in which they occur in the stomach, upon their action. He used 20-gram frogs (*Rena temporaria*), exposing the heart and after injecting 1 c. c. of the solution to be tested, noted the time of the appearance of systolic standstill.

Kochman^b showed that five infusions of digitalis made from leaves obtained from different sources possessed different actions upon the blood pressure of dogs, only two of them producing the true digitalis effect of increased blood pressure and lessened pulse rate.

In a research to determine the uniformity of the preparations of digitalis and strophanthus which were upon the market Edmunds^c examined seventeen preparations of the tinctures of digitalis and six of strophanthus. Although many of these were said to be physiologically standardized they showed great variation, two preparations (standardized) from one manufacturer having toxicities in the ratio of 1 to 2. Four nonstandardized preparations from one manufacturer varied as 1 to 4.

The method employed to standardize the drugs was the same as has been used in the pharmacological laboratory of the University of Michigan for a number of years and is essentially the same as that employed by Famulener and Lyons,^d the only difference being that as an end reaction complete systolic stoppage of the heart is used, not only of the ventricle, as in the Famulener and Lyons method, but also of the auricles.

In his comparison of various tinctures of strophanthus which were on the market Hatcher^e adopted Frankel's method of examination; that is, the amount necessary to produce systolic standstill of the frog's heart in about one hour, comparing the doses when calculated

^a Löwy, Wien klin. Wchnschr., 1906, XIX, 1157.

^b Kochman, Bull. Soc. de Med. de Gand., 1906, LXXIII, 95.

^c Edmunds, J. A. M. A., 1907, XLVIII, 1744.

^d Famulener and Lyons, Proc. Am. Pharm. Ass., 1902, L, 415.

^e Hatcher, J. A. M. A., 1907, XLVIII, 1177.

on the basis of 100 grams frog's weight. He also compared their action upon cats and dogs, these reacting by vomiting. He suggested on account of the regularity of the appearance of this symptom, that it might be thought of as an index of the potency of the drug but because of the variability of the reaction of the vomiting center he "considered it better to determine the amount necessary to produce systolic standstill which is, of course, promptly followed by death."

In his article "Ueber die physiologische Wertbestimmung von Arzneimitteln" Gottlieb^a, after discussing the work of Frankel, Zeigenbein, and Bühner upon physiological standardization, mentions the results of his investigation upon the uniformity of digitalis leaves used in the clinics around Heidelberg, showing that they varied as much as fourfold. He calls attention to the necessity of a government institution where such preparations can be examined, a fact to which attention has been called by several earlier writers.

In order to obtain a convenient method of designating the strength of preparations he suggests the adoption of a standard "unit," using the term in the same way as it is used in connection with sera work. For such a unit he has adopted the following: "The smallest amount of the solution which will call forth systolic standstill of the heart of a *R. temporaria* of 30 grams weight in thirty minutes exactly." In an infusion freshly prepared from 1 gram of good digitalis leaf powder there must be 30 to 40 units; the strongest leaves may contain 120 units.

He further points out that such a comparison on the frog's heart is only possible when made with similar active constituents, such as we have in the leaves, infusion, and tincture of digitalis, but could not hold good with dissimilar constituents as, for instance, a comparison of *strophanthus* with digitalis. A further fact which he calls attention to is that, in the methods usually employed in which the heart is to be brought to a systolic standstill in a certain short time, a strong solution of a substance, absorbed with difficulty, would appear weaker than a weak solution of easily absorbable substances.

Sowton^b undertook to examine the activity of twenty-six specimens of the tincture of digitalis by means of perfusing the hearts of rabbits. He chose animals weighing 3 or 4 pounds each, and, using the coronary vessels, perfused the right ventricle with a solution of digitalis of a strength of 1 to 200 made up in Locke's or Ringer's solution. From his results he grouped the preparations into two classes, "strong" and "weak," but later found that such a classification was impossible, as five of his specimens upon which seventeen experiments had been carried out were placed some in one group and some in the other, and yet they were probably alike, having been made in exactly the same

^a Gottlieb, München. med. Wchnschr., 1908, LV, 1265.

^b Sowton, Brit. M. J., London, 1908, No. 2458, 310.

manner from the same lot of leaves. The results indicated the practical worthlessness of the method, as rabbits' hearts evidently exhibit marked variations.

Lutzkaja^a published a critical study of the Focke method of standardization which he thinks is preferable to the one-hour method which, according to his views, is too inexact. He carried out the experiments according to Focke's directions with the exception that he used September and October frogs.

In his first experiments, with 0.5 milligram doses of digitoxin injected into frogs of different weights, he obtained toxic values showing as great variations as from 1.9 to 8.3 with an average of 4.5. For his second experiments he estimated the doses so as to stop the heart in about ten minutes, and by this means the results were much more uniform, differing only 80 per cent. In a third experiment his results varied still less, only 65 per cent. His conclusion is that, in spite of some irritating individual variation, if a sufficient number of experiments are carried out useful results may be obtained. He urges as an objection to the "short-time methods" that they might not give sufficient time for all the poison to be absorbed and by this means a very active preparation, absorbed with difficulty, would appear weaker than a weak preparation containing easily absorbable constituents.

His results show that digitoxin and digitalinum verum do not give the same ratio on frogs as their relative doses appear to indicate that they possess in man; in some preparations of digitalis he suggests there might be a great deal of digitoxin, but in others not as much, and while they might show the same effect on frogs they would not on man. He therefore thinks such a condition would render the standardization of the leaves on frogs of little value.

Practically every worker upon this subject has employed the frog in some way or other as a means of standardizing the preparations of the drugs under consideration and the results obtained upon this animal have been confirmed in some cases by control experiments carried out, usually upon the blood pressure, upon the higher animals. However, in 1908 Reed and Vanderkleed^b introduced a method, using guinea pigs, as they object to the frog because the reaction of this animal is very irregular, being affected by the season of the year, the species, etc. They also point out that the action upon the heart is a toxic effect, a determination of the lethal dose, and therefore they substitute for the toxic dose in frogs the toxic dose in guinea pigs. To make the assay they prepare their tinctures by evaporating off the alcohol and diluting the residue with water. Progressively increasing doses are then injected subcutaneously into guinea

^a Lutzkaja, Arch. internat. de Pharmacod, Gand et Par., 1908, XVIII, 77.

^b Reed and Vanderkleed, Am. J. of Pharm., 1908, LXX, 110.

pigs of 240 grams weight until the amount is found which will kill the animal in one and one-half to two hours. Their standard dose then, which they confirm by injecting like amounts into five or six animals, is that amount which would kill a guinea pig of 240 grams weight in one and one-half to two hours. They carried out a series of experiments to compare the digitoxin content of tinctures with the physiological activity. These results are tabulated on page 9.

EXPERIMENTAL WORK.

As will be seen from a study of the literature that has been given there are essentially three methods used for the biological assay of the members of the digitalis series, the others being merely modifications departing more or less widely from what we may consider the primary groups. These may be classified as follows: A toxic method, in which frogs, guinea pigs, or some of the higher animals are used; second, a method using the frog's heart, which is perfused in some cases while in others it is simply exposed and systolic standstill is watched for (this in Focke's method is reached in from seven to twenty minutes, while in others a longer interval of one or two hours is allowed); the third class includes those methods which aim at a comparison by means of the relative effects upon the blood pressures of some of the higher animals.

One of the objects of the present study has been to examine into the results of these various methods to find if possible if one possessed a marked advantage over the others, and, most important of all, to see whether the different methods would give anything approaching uniform results in a comparative study of a number of digitalis preparations, some of which have been made according to the pharmacopœial requirements, while others had been manufactured according to some special method devised by individual pharmaceutical houses. A study of these preparations constitutes an important part of the work, but was not the primary object of the research.

With these objects in view we have examined nine preparations of digitalis, namely: Fluid extracts prepared according to the U. S. Pharmacopœia, VIII, by Messrs. Parke, Davis & Co., Detroit; Sharpe & Dohme, Baltimore; Nelson, Baker & Co., Detroit; Hance Brothers & White, Philadelphia. In addition to these we examined several proprietary preparations as follows: Three specimens of Digitalone, prepared by Parke, Davis & Co.; a fat-free tincture of digitalis (Digitol), prepared by H. K. Mulford & Co., Philadelphia; Digitalis, Specific Medicine, manufactured by Lloyd Brothers, Cincinnati; a Concentrated Tincture of Digitalis (1 to 4), prepared by Burroughs, Wellcome & Co., London, and finally a purified "Normal Tincture," prepared by William S. Merrell & Co., Cincinnati.

Digitalone is said to be a "nonalcoholic permanent solution of digitalis" corresponding in strength to the U. S. Pharmacopœia tincture and physiologically standardized. The manufacturers state that

Digitol is a preparation of tincture strength made from digitalis leaves from which the fixed and volatile oils have been removed. It is "assayed, tested physiologically," and is standardized to contain 0.025 gram digitoxin in 100 c. c. - Digitalis (Specific Medicine) is made from fresh digitalis leaves, and is of such a strength that 480 grains of the drug are contained in each fluid ounce of "80 per cent absolute alcohol." Concentrated Tincture of Digitalis (1 to 4) is said to be physiologically standardized and is of such a strength that 1 c. c. added to 4 c. c. dilute alcohol makes a preparation corresponding in strength to the U. S. Pharmacopœia tincture. Purified Normal Tincture is said to be a standardized neutral tincture of prime digitalis freed from irritating fats and oils.

It was desired for the sake of comparison that all experiments with these various preparations be carried out upon the basis of the official tincture strength. No difficulty was experienced in doing this except with Merrell's Normal Tincture, the name of which might suggest that it was a 10 per cent preparation, but for reasons to be considered later, the dose prescribed, etc., it was considered to correspond to a fluid-extract strength. Accordingly a measured quantity of each preparation (excepting Digitol and Digitalone) was taken and after evaporating off the alcohol over a water bath it was diluted to ten times the original volume with physiological salt solution. Digitol was evaporated to free it from the contained alcohol and then diluted to the original volume only. Digitalone, being nonalcoholic, was not evaporated excepting in some experiments when it was concentrated in order to avoid such a large bulk of fluid as the doses given required. In all cases resinous bodies, precipitated by the evaporation of the alcohol and the addition of the salt solution, were injected in suspension to insure the introduction of any active bodies which might be carried down by their precipitation.

For the sake of uniformity the following abbreviations have been adopted to designate the above preparations in all of the tables which follow:

Digitol, bottle No. 1 = Mulford No. 1.

Digitol, bottle No. 2 = Mulford No. 2.

Normal Tincture Digitalis = Merrell.

Concentrated Tincture Digitalis = B., W. and Co.

Specific Medicines, Digitalis = Lloyd Bros.

Nelson Baker and Co., Fluid Extract Digitalis = N., B. and Co.

Sharpe and Dohme, Fluid Extract Digitalis = S. and D.

Hance Bros. and White, Fluid Extract Digitalis = H. B. and W.

Parke, Davis and Co., Fluid Extract Digitalis = P., D. and Co.

Parke, Davis and Co., Digitalone bottle No. 1 = Digitalone No. 1.

Parke, Davis and Co., Digitalone bottle No. 2 = Digitalone No. 2.

Parke, Davis and Co., Digitalone bottle No. 3 = Digitalone No. 3.

MINIMUM LETHAL DOSE METHOD OF ASSAY.

The method adopted for examination and the animals employed by us as illustrating the toxic methods of assay were as follows:

Mice.—White mice, kept under the same conditions and varying in weight from 15 to 25 grams, were used. The drug was injected hypodermically beneath the skin of the back, the dose being calculated at so many milligrams per gram of body weight and so diluted that a dose of 1 c. c. was not exceeded in any case. The mice were then watched and the death or survival of the animal noted. The data thus obtained (as were the results in all subsequent series of experiments) were confirmed by injecting a second series of mice several days later. The results of these tests are given in Table I.

TABLE I.—*Determination of the minimum lethal dose per gram body weight for white mice; subcutaneous injection.*

[Survived = -; dead = +.]

MULFORD NO. 1.

Number of animals used. ^a	Dose.	Results.
	<i>mgm.</i>	
1.....	2	-
4.....	3	-
5.....	4	+
3.....	5	+
3.....	6	+

MERRELL.^b

1.....	3	-
1.....	4	-
2.....	5	-
1.....	5	+
3.....	6	+
2.....	7	+

B. W. AND CO.

3.....	3	-
2.....	4	+
1.....	5	+
1.....	6	+
2.....	7	+

H. B. AND W.

3.....	6	-
1.....	7	-
3.....	7	+
2.....	8	+
1.....	9	+

DIGITALONE NO. 1.

1.....	10	-
1.....	19	-
1.....	20	-
1.....	22	+
1.....	25	+
1.....	28	+
1.....	30	+

LLOYD BROS.

Number of animals used. ^a	Dose.	Results.
	<i>mgm.</i>	
2.....	18	-
2.....	19	-
2.....	20	-
1.....	20	+
2.....	21	-
1.....	21	+
1.....	22	-
2.....	22	+
3.....	23	-
2.....	23	+
2.....	24	-
4.....	24	+

N. B. AND CO

3.....	7	-
2.....	8	-
2.....	8	+
3.....	9	+
1.....	11	+

S. AND D.

2.....	6	-
2.....	7	-
4.....	8	-
1.....	8	+
2.....	9	-
3.....	9	+
1.....	10	-
3.....	10	+

P., D. AND CO.

2.....	3	-
3.....	4	+
3.....	4	-
2.....	5	+
3.....	5	-
2.....	6	+
3.....	6	-
2.....	7	+
3.....	7	-
4.....	8	+

^a The heading "Number of animals used" refers to the number of animals which received the dose indicated in the second column.

^b Dose calculated on the basis that preparation was of fluid extract strength.

TABLE I.—*Determination of the minimum lethal dose per gram body weight for white mice; subcutaneous injection—Continued.*

SUMMARY.

Minimum lethal dose for mice per gram body weight.

Preparation.	Milli-grams.
Mulford (digitol).....	4
B. W. and Co. (concentrated tincture).....	4
Merrell (normal tincture).....	6
H. B. and W. (fluid extract).....	7
P., D. and Co. (fluid extract).....	8
N., B. and Co. (fluid extract).....	9
S. and D. (fluid extract).....	9
Digitalone No. 1 (P., D. and Co.).....	22
Lloyd Bros. (specific medicine).....	24

Guinea pigs.—Guinea pigs of about the same weight were injected beneath the skin of the abdomen with the drugs to be tested. The dose was reckoned according to the weight of the animal and the preparations were so diluted as to make the bulk of the fluid injected between 1 and 2 c. c. The results of these experiments are recorded in Table II.

TABLE II.—*Determination of the minimum lethal dose for guinea pigs—subcutaneous injection.*

[Survived = —; dead = +.]

MULFORD NO. 1.

Number of animals used. ^a	Dose.	Result.
	<i>mgm.</i>	
1.....	0.56	—
1.....	.625	—
2.....	.65	—
1.....	.70	—
1.....	.70	+
1.....	.75	+
1.....	.80	+

MERRELL.

1.....	0.40	—
2.....	.50	—
4.....	.50	+
3.....	.60	—
5.....	.60	+
1.....	.65	+
2.....	.70	+

B. W. AND CO.

1.....	0.25	—
2.....	.30	—
1.....	.35	—
2.....	.35	+
1.....	.40	+
1.....	.55	+
1.....	.68	+

LLOYD BROS.

Number of animals used. ^a	Dose.	Result.
	<i>mgm.</i>	
2.....	0.70	—
2.....	.80	—
2.....	.80	+
2.....	.90	—
3.....	.90	+
1.....	1.00	—
2.....	1.00	+
1.....	1.50	+
1.....	2.00	+

DIGITALONE NO. 1.

1.....	2.00	—
1.....	4.00	—
1 ^b	5.00	+

N., B. AND CO.

1.....	0.50	—
1.....	.70	—
2.....	.80	—
2.....	.80	+
3.....	.90	+
2.....	1.00	+
1.....	1.20	+

^a This heading refers to the number of animals which received the dose indicated in the second column.^b Guinea pig, weight 250 grams, injected with 12.5 c. c., digitalone No. 1. No digitalis symptoms whatever appeared, the animal passing at once into a comatose condition. The respiration became weaker and finally ceased. Cause of death (?).

TABLE II.—*Determination of the minimum lethal dose for guinea pigs—subcutaneous injection—Continued.*

DIGITALONE NO. 3.			P., D. AND CO.		
Number of animals used.	Dose.	Result.	Number of animals used.	Dose.	Result.
	<i>mgm.</i>			<i>mgm.</i>	
1.....	0.90	—	1.....	0.50	—
1.....	1.50	a—	1.....	.60	—
			1.....	.70	—
			2.....	.70	+
			2.....	.80	+
H. B. AND W.			S. AND D.		
1.....	0.30	—	1.....	0.70	—
2.....	.40	—	3.....	.80	—
2.....	.50	+	1.....	.80	+
1.....	.70	+	1.....	.90	—
1.....	1.00	+	4.....	.90	+

a No symptoms.

Digitalone No. 3 was used in injecting two guinea pigs, one receiving 0.9 milligram and the other 1.5 milligrams per gram weight. Neither of these animals showed any symptoms whatever excepting that they were somewhat less active than normal.

SUMMARY.

Preparation.	M. L. D. ^a
	<i>mgm.</i>
B. W. and Co.....	0.35
H. B. and W.....	.50
Merrell.....	.60
Mulford No. 1.....	.70
P., D. and Co.....	.70
N., B. and Co.....	.90
S. and D.....	.90
Lloyd Bros.....	.90
Digitalone No. 1.....	5.00(?)
Digitalone No. 3.....	b 1.50

^a M. L. D.=minimum lethal dose.^b Lived.

Cats.—The toxic dose was determined for these animals in the course of the blood-pressure experiments. After the initial injection of 1 c. c. of the 10 per cent solution, further injections of 0.5 c. c. each were administered at intervals of not less than 5 minutes, artificial respiration being maintained so that the toxic action was due to an effect upon the heart rather than upon the medulla. This was thought desirable because in some of the earlier experiments the respiration was observed to have failed, although a good circulation was being maintained, while in others the animal would make apparently normal respiratory efforts after the heart had stopped and the blood pressure had fallen to zero. The toxic doses were compared on the basis of the number of milligrams of the drug used per kilogram of body weight of the animal. The results of this series of experiments and the average for each drug used are given in the last two columns of Table III.

TABLE III.—*Determination of blood pressure and minimum lethal dose for cats, intravenous injection. Fluid extracts diluted to 10 per cent strength.*

	Heart rate.	Blood pressure.	Percentage increase in blood pressure.	Lethal dose.	Lethal dose per kilogram, body weight.
N., B. AND CO.					
August 4, 1908, cat, 3,800 grams:				c. c.	mgm.
Normal.....	126	55			
After 1 c. c.....	150	122	122	7	184
September 9, 1908, cat, 3,780 grams:					
Normal.....	90	38			
After 1 c. c.....	90	60	58	6	158
September 9, 1908, cat, 2,930 grams:					
Normal.....	120	36			
After 1 c. c.....	120	78	116	7	235
Average.....			99		192
MULFORD NO. 2.					
August 6, 1908, cat, 1,380 grams:					
Normal.....	162	60			
After 1 c. c.....	186	140	133	2	145
August 6, 1908, cat, 1,870 grams:					
Normal.....	192	68			
After 1 c. c.....	186	86	27	4	214
September 4, 1908, cat, 3,250 grams:					
Normal.....	198	66			
After 1 c. c.....	174	84	27	7	215
September 11, 1908, cat, 2,870 grams:					
Normal.....	180	94			
After 1 c. c.....	180	158	68	6	208
Average.....			64		195
DIGITALONE NO. 2.					
August 5, 1908, cat, 1,800 grams:					
Normal.....	174	66			
After 1 c. c.....	168	100	52	9	500
September 9, 1908, cat, 2,500 grams:					
Normal.....	150	38			
After 1 c. c.....	160	60	58	15	600
Average.....			55		550
B. W. AND CO.					
August 5, 1908, cat, —:					
Normal.....	198	80			
After 1 c. c.....	210	104	30		
August 7, 1908, cat, 1,150 grams:					
Normal.....	180	39			
After 1 c. c.....	186	74	90	2	174
September 4, 1908, cat, 3,500 grams:					
Normal.....	138	50			
After 1 c. c.....	138	66	32	5	143
Average.....			51		158
P., D. AND CO.					
August 5, 1908, cat, 1,600 grams:					
Normal.....	114	40			
After 1 c. c.....	126	55	38	3	187
September 5, 1908, cat, 3,220 grams:					
Normal.....	174	56			
After 1 c. c.....	162	76	36	5	155
Average.....			37		171
S. AND D.					
August 7, 1908, cat, 1,150 grams:					
Normal.....	216	94			
After 1 c. c.....	210	112	19	2	174
September 5, 1908, cat, 1,690 grams:					
Normal.....	144	40			
After 1 c. c.....	114	64	60	5	296

TABLE III.—*Determination of blood pressure and minimum lethal dose for cats, intravenous injection. Fluid extracts diluted to 10 per cent strength—Continued.*

	Heart rate.	Blood pressure.	Percentage increase in blood pressure.	Lethal dose.	Lethal dose per kilo-gram, body weight.
S. AND D.—continued.					
September 8, 1908, cat, 2,880 grams:				c. c.	mgrm.
Normal.....	158	56			
After 1 c. c.....	162	74	32	6	208
September 8, 1908, cat, 3,800 grams:					
Normal.....	162	64			
After 1 c. c.....	156	84	31	11	289
Average.....			35		242
H. B. AND W.					
August 4, 1908, cat, 2,400 grams:					
Normal.....	162	58			
After 1 c. c.....	204	100	72	4	166
September 10, 1908, cat, 3,050 grams:					
Normal.....	220	68			
After 1 c. c.....	190	78	15	7	229
September 10, 1908, cat, 3,900 grams:					
Normal.....	120	50			
After 1 c. c.....	120	62	24	9	231
September 11, 1908, cat, 3,620 grams:					
Normal.....	130	70			
After 1 c. c.....	140	85	21	9	249
Average.....			33		219
MERRELL.					
August 4, 1908, cat, 3,600 grams:					
Normal.....	138	54			
After 1 c. c.....	132	70	30	7	194
September 12, 1908, cat, 2,540 grams:					
Normal.....	200	90			
After 1 c. c.....	210	104	16	7	275
September 16, 1908, cat, 2,800 grams:					
Normal.....	140	54			
After 1 c. c.....	140	72	33	8	286
Average.....			26		252
DIGITALONE NO. 3.					
August 6, 1908, cat, 1,600 grams:					
Normal.....	138	70			
After 1 c. c.....	120	84	20	4	250
August 6, 1908, cat, 1,930 grams:					
Normal.....	120	46			
After 1 c. c.....	108	60	31	6	310
Average.....			26		280
LLOYD BROS. ^a					
August 5, 1908, cat, 2,000 grams:					
Normal.....	168	66			
After 1 c. c.....	168	84	27	8	400
September 11, 1908, cat, 2,730 grams:					
Normal.....	130	52			
After 1 c. c.....	130	63	21	13	476
Average.....			24		438
DIGITALONE NO. 1.					
August 5, 1908, cat, 1,800 grams:					
Normal.....	180	68			
After 1 c. c.....	210	48	b 29		
September 5, 1908, cat, 3,220 grams:					
Normal.....	160	60			
After 1 c. c.....	190	50	b 17		
Average.....			b 23		

^a Specific medicine. Evaporated at room temperature and diluted to 10 per cent strength with salt solution.^b Per cent fall.

TABLE III.—*Determination of blood pressure and minimum lethal dose for cats, intravenous injection. Fluid extracts diluted to 10 per cent strength—Continued.*

SUMMARY OF TOXIC DOSES FOR CATS (AVERAGES).

Preparation.	Milli-grams.
B. W. and Co.....	158
P., D. and Co.....	171
N., B. and Co.....	192
Mulford No. 2.....	195
H. B. and W.....	219
S. and D.....	242
Merrell.....	252
Digitalone No. 3.....	280
Lloyd Bros.....	438
Digitalone No. 2.....	550

Frogs.—Finally the toxic dose on frogs was found according to Houghton's^a method (see p. 16). The frogs (*R. pipiens*, Schreber, Syn. *R. virescens* and *halecina*) were unpacked as soon as they arrived and placed in a large cage through the end of which flowed fresh water. They were only brought to the experimental room when needed and injected late in the afternoon. They were then placed in separate jars and early the following morning the death or survival of each animal was noted. The results of experiments in which the lethal doses of four of the digitalis preparations were determined are given in Table IV.

TABLE IV.—*Determination of the minimum lethal dose for Rana pipiens, twelve-hour method.*

[Survived = —, dead = +. Dose per gram body weight.]

MULFORD NO. 2.

Series.	Dose.	Result.
	c. c.	
1.....	0.016	—
	.018	—
	.020	+
2.....	.019	+
	.020	+
	.020	—
3.....	.020	+
	.020	+
	.020	—

B. W. AND CO.

1.....	0.010	—
	.012	—
	.014	—
2.....	.014	+
	.016	+
	.018	+
3.....	.015	+
	.015	+
	.015	+

P., D. AND CO.

Series.	Dose.	Result.
	c. c.	
1.....	0.024	—
	.026	—
	.028	—
2.....	.030	+
	.032	—
	.034	+
3.....	.029	+
	.030	+
	.032	+
4.....	.029	+
	.029	+
	.029	+

S. AND D.

1.....	0.025	—
	.026	+
	.027	—
2.....	.026	—
	.027	+
	.028	+
3.....	.027	+
	.027	+
	.027	—

^a Houghton, J. Am. Med. Ass., Chicago, 1898, XXXI, 959.

TABLE IV.—*Determination of the minimum lethal dose for Rana pipiens, twelve-hour method—Continued.*

SUMMARY.

Preparation.	M. L. D. ^a
B. W. and Co.	c. c. mgm.
Mulford No. 2.	0.015=1.5
S. and D.020=2.0
P., D. and Co.027=2.7
	.029=2.9

^a M. L. D.=minimal lethal dose.

Factors modifying effect.—Our experiences with the various factors which are supposed to influence the reaction of the frogs may be briefly summarized here.

Weight.—In regard to the weight of the animal many workers have apparently very largely ignored this factor, while others have made only an approximate allowance for it. For instance, Focke says to use frogs weighing from 25 to 30 grams, while others merely say "large" frog or "medium" or "small," as the case may be. In our experience, which covers some years, we have always weighed the animals fairly accurately, within the limits of 1 gram, and then calculated the dose per gram body weight.^a This seems not to be absolutely necessary, judging from the reports of several writers quoted, but we think that it can not help but insure greater uniformity in the results, especially when there are certain factors such as idiosyncrasy which can not possibly be allowed for.

Sex.—Our experiences agree with those of Focke that unless it is in the springtime there is no particular difference in the reaction obtained from male and female frogs.

Season.—The effect of the season of the year upon the conditions of the frogs seems to be pretty generally recognized. Both Moschcowitsch and Dixon point out that the frogs are most active in the spring. The question has been most fully considered by Focke, who says that on account of the seasonal variations only summer frogs should be employed, as they not only react differently at this time but there is very much less variation in their reaction. According to a later research,^b if they are to be used at any other season, they should themselves be standardized by testing them against a digitalis preparation of known value and using the temperature factor which will give the preparation its standard "V" as previously determined. The introduction of this factor, however, we believe to be entirely unnecessary excepting that comparative experiments should be car-

^a In our former work we used as a standard for comparison doses calculated on the basis of a 20-gram frog, but in this work we have compared the preparations upon the basis of 1-gram body weight as being simpler.

^b Focke, Arch. d. Pharm., 1907, CCXLV, 646.

ried out at the same temperature. That a given preparation should show a worth of 5 at one time and only 3 at another seems of very little importance if its keeping qualities are known to be good. All that is necessary is to keep such a preparation in stock and, at any time when an assay is to be made, to redetermine its activity and then make the unknown conform to the value found. The only essential is that the known and the unknown digitalis preparation be tested at the same temperature.

Focke^a carried out a series of experiments especially designed to show the effect of season. (The temperature factor probably played some part in the results.) He employed a digitalis powder which had been very thoroughly dried and carefully preserved. During April, May, and the early part of June the average of all experiments gave the powder a worth of 2.66. From the last of June to the end of September a V of 4.36; during October, a V of 5, and on November 20 a V of 3.3. These variations he ascribes to the nutrition of the frogs which is lowest in the spring and gradually improves during the summer, reaching its highest point just before the winter sets in, when it falls off sharply until it reaches the low point in the spring. He also says in a later paper that in the spring the frogs react weakly, and this is supported by the results of experiments in which he shows that the temperature must be increased in order to obtain the same values for the same preparation as at other seasons. His tables show that reacting weakly the frogs require a larger dose of the drug or an increase in the temperature of the operating room to produce the same effect and therefore give a lower V to the specimen of leaves examined.

The effect of a lowered nutrition in increasing the resistance to the drug is rather surprising, especially as our experiments, while not as complete as Focke's, show exactly the opposite effect, viz, that in the summer when the animals are most vigorous they require a larger dose to produce systolic standstill of the heart. We worked with a different variety of frogs from those Focke employed, but it would hardly be expected that this factor should make such a fundamental difference. Our experience may be summarized as follows:

The U. S. Pharmacopœia tincture examined by Edmunds^b in 1907 required a dose of from 0.16 to 0.20 c. c. to produce systolic standstill in one hour. In experiments carried out in August, 1908, frogs belonging to the same species (*R. pipiens*) and of the same size required 0.40 to 0.50 c. c. to produce the same effect.

To be still more exact, in April, 1907, a Parke, Davis and Co. tincture required 0.15 c. c. to produce the end reaction described above; in 1908 one of their fluid extracts made to correspond to tincture

^a Focke, Arch. d. Pharm., 1903, CCXLI, 678. Ther. d. Gegenw., 1904, XLV, 251.

^b Edmunds, J. Am. Med. Ass., Chicago, 1907, XLVIII, 1744.

strength required 0.42 c. c. As these preparations are both physiologically assayed to a definite strength, the difference must be ascribed to the variability of the reaction of the frogs. As a means of demonstrating the uniformity of these two preparations mentioned, we might say that the 1907 tincture corresponded in strength to a tincture made in the laboratory at Ann Arbor from leaves obtained from Parke, Davis and Co., while their 1908 preparation is practically the same strength as U. S. Pharmacopœia fluid extracts made by other firms and which were examined at the same time, the results being given in the table on page 44.

In striking contrast to these views are the results of some of Houghton's^a assays, which were carried out to ascertain if a standard tincture would deteriorate in a year if kept under proper conditions. His two tables, which we give below, show not only that the standard preparations do not deteriorate, but also, what is equally important and interesting, that frogs react exactly the same at all times of the year.

TABLE III A.—*Standard strophanthus.*

Date.	Toxic dose.
July 6, 1897.....	0.00015
October 19, 1897.....	.00015+
December 20, 1897.....	.00015
February 23, 1898.....	.00015—
April 25, 1898.....	.00015

TABLE III B.—*Concentrated strophanthus.*

Date.	Toxic dose.
July 28, 1897.....	0.0000037
November 10, 1897.....	.0000037

Ziegenbein also did not think that season made much difference in the susceptibility of frogs. However, it may be said that any errors due to differences in the reaction of the frogs dependable upon season can be avoided, in the first place, by standardizing the frogs with reference to the temperature of the operating room after the manner of Focke, and, second and more simply, these differences may be avoided by always assaying a standard solution of digitalis, which is kept under proper conditions at the same time that the unknown solution is examined.

FROG-HEART METHODS OF ASSAY.

According to our classification, the second group is concerned with an action upon the frog's heart as a means of measuring the comparative strengths of the different preparations. In these methods the

^a Houghton, J. Am. Med. Ass., 1898, XXXI, 959.

end reaction is the stoppage of the frog's heart in systole, the chief differences between the various methods being dependant upon variations in the time factor.

The one-hour method.—In this method the frogs are secured and kept in the manner already described, weighed, and such a dose is injected that the heart will be found in complete systolic contraction at the end of exactly sixty minutes. The drug, properly diluted so as to make a volume of 0.5 to 1 c. c., is injected into the anterior lymph sac by means of a glass pipette. Shortly before the hour is up the frog is pithed, tied to a frog board, and the heart is exposed in the usual manner. If the heart is still beating, the dose has been too small and must be increased in subsequent trials. In the first series of frogs doses are chosen with wide limits, which in a second and third series of animals are narrowed down until the smallest amount of the drug which will produce systolic standstill in one hour is found. Usually three series of frogs are sufficient to assay one preparation, but in case of any irregularity in the reaction of any of the frogs a fourth or even a fifth series may be necessary. The results of our assay of the different preparations are given in Table V.

TABLE V.—*Determination of the systolic stoppage of the heart of Rana pipiens in one hour—Drug injected into abdominal lymph sac. The doses given are in cubic centimeters per gram body weight.*

MULFORD NO. 1.

Number of animals used.	Dose.	Result.
	c. c.	
1.....	0.009	—
1.....	.01	—
3.....	.011	—
1.....	.0115	—
3.....	.012	+
1.....	.014	+
1.....	.016	+

B. W. AND CO.

Number of animals used.	Dose.	Result.
	c. c.	
1.....	0.018	—
1.....	.019	—
1.....	.020	a +
1.....	.020	+
1.....	.021	+
1.....	.022	+

DIGITALONE NO. 3.

	Dose.	Result.
2.....	0.035	—
1.....	.037	—
1.....	.038	—
1.....	.039	+
1.....	.040	—
2.....	.040	+
1.....	.041	—
1.....	.042	+

LLOYD BROS.

	Dose.	Result.
1.....	0.027	—
3.....	.028	—
3.....	.029	—
4.....	.030	+

DIGITALONE NO. 2.

	Dose.	Result.
1.....	0.025	—
1.....	.032	—
1.....	.040	—
1.....	.050	—
1.....	.105	—
1.....	.120	(b)

S. AND D.

	Dose.	Result.
1.....	0.025	—
1.....	.026	—
1.....	.026	+
1.....	.027	—
3.....	.027	+
1.....	.028	—
3.....	.028	+
1.....	.029	+

MULFORD NO. 2.

	Dose.	Result.
1.....	0.014	—
2.....	.015	—
1.....	.016	—
4.....	.016	+
1.....	.017	+

a Diastole.

b Diastole, later beating.

TABLE V.—*Determination of the systolic stoppage of the heart of Rana pipiens in one hour—Drug injected into abdominal lymph sac. The doses given are in cubic centimeters per gram body weight—Continued.*

MERRELL.			H. B. AND W.		
Number of animals used.	Dose.	Result.	Number of animals used.	Dose.	Result.
2.....	c. c. 0.022	—	2.....	c. c. 0.022	—
2.....	.023	—	1.....	.023	—
1.....	.023	+	2.....	.024	—
2.....	.024	—	2.....	.025	+
3.....	.024	+	1.....	.026	—
5.....	.025	+	2.....	.026	+
1.....	.026	+	1.....	.027	+
N., B. AND CO.			P., D. AND CO.		
1.....	0.020	—	1.....	0.018	—
2.....	.021	—	1.....	.019	—
1.....	.021	+	1.....	.020	—
1.....	.022	+	2.....	.020	+
1.....	.022	+	2.....	.021	—
1.....	.023	+	3.....	.021	+
1.....	.025	+	3.....	.022	+
SUMMARY.					
Preparation.				Dose.	
				c. c. mgm.	
Mulford No. 1.....				0.012=1.2	
Mulford No. 2.....				.016=1.6	
B. W. and Co.....				.020=2.0	
P., D. and Co.....				.021=2.1	
N., B. and Co.....				.022=2.2	
Merrell.....				.024=2.4	
H. B. and W.....				.025=2.5	
S. and D.....				.027=2.7	
Lloyd Bros.....				.030=3.0	
Digitalone No. 3.....				.040=4.0	
Digitalone No. 2.....					

"*Focke*" method.—The second method upon the frog's heart which we employed was that of Focke, modified, however, in one or two important particulars. In the first place, we pithed all the frogs, while Focke does not do this until the experiment is over. It is absolutely essential that this should be done for purely humanitarian reasons, and if this operation interferes with the accuracy of his method then the method can not be used. As a matter of fact, this was done very carefully so as not to lose any blood, and the piece of sharpened wood was left in the brain cavity so as to prevent hemorrhage. The other modification was patterned after Wang, who found it was hard to determine when the ventricle may be said to have come to a permanent systolic standstill. We found exactly the same difficulty, and so adopted Wang's modification of watching for the stoppage of the circulation. Wang does not mention how he determines this, but the method we used was to watch with the microscope the stoppage of the circulation in the web of the foot. This itself is not always satisfactory, because in some animals, due to

some unknown condition, very little movement will be found in the blood in the web vessels. The most important factor in the condition of the peripheral circulation seemed to be whether any hemorrhage whatever had occurred during the operation. If even a drop of blood had been lost its loss appeared to be shown by the poor circulation in the web. An important precaution we adopted was, after selecting the field which showed the most favorable circulation, to note the direction of the flow in the main streams. If this was not done, after the heart stopped or had become very weak the blood would frequently flow in the reverse direction and continue doing so for a long time. If it was not known that the blood was no longer going in the normal direction it would be supposed that the circulation had not ceased.

In most cases it was very hard to tell exactly when the circulation did actually stop, because when the heart became weak the blood would stop flowing for a short period, to be followed by a renewal of the flow just as soon as enough pressure was obtained in the supplying arteries to overcome peripheral resistance. Both end reactions, either stoppage of the heart or of the circulation, are very indefinite, in our opinion, but probably if a sufficient number of experiments are carried out a fairly definite idea of the relative strength of the preparations can be obtained.

It is very essential in this method if a comparison of different preparations is to be carried out not merely to choose any dose which will stop the heart at any time between seven and twenty minutes, because quite different values are obtained if a dose is given which will stop all the hearts in eight minutes or in say eighteen minutes. As we found, and as Focke shows in his tables, the shorter times give higher values, so that in comparing two preparations it would be necessary to have the hearts stop at some average time, ten or twelve minutes, or to so regulate the doses that two hearts will stop in about eight minutes, two in twelve or thirteen, and two in eighteen. We adopted this rule and in this way a fairly good average is attained. However, even with these precautions, we believe that this method allows of greater variations and inaccuracies than any other method we employed. The results of the determination of the toxic dose of the different digitalis preparations by this method are given in Table VI.

TABLE VI.—*Determination of toxic dose for Rana pipiens, Focke method—drug injected into leg lymph sacs.*

Time is noted when circulation in web of foot stops. Dose is calculated per gram body weight, animals weighing between 25 and 30 grams each

MULFORD NO. 1.			N., B. AND CO.		
Dose.	Time.	Value (V).	Dose.	Time.	Value (V).
c. c.	Min.		c. c.	Min.	
0.020.....	18	2.8	0.015.....	27
.020.....	18	2.8	.020.....	18	2.7
.020.....	14	3.6	.020.....	17	2.9
.0225.....	9	4.9	.0225.....	10	4.4
.0225.....	12	3.7	.025.....	20	2.0
.023.....	11	3.9	.026.....	12	3.2
.025.....	9	4.4	.027.....	15	2.5
.025.....	9	4.4	.030.....	13½	2.5
Average.....		V=3.8	.035.....	10	2.9
MERRELL. ^a			Average.....		
					V=2.9
			H. B. AND W.		
0.035.....	20	1.4	0.0325.....	14	2.2
.035.....	15	2.0	.0325.....	15	2.0
.036.....	16	1.8	.033.....	13	2.3
.0375.....	13	2.0	.035.....	12	2.4
.0375.....	13	2.0	.035.....	11	2.6
.038.....	12	2.2	.0375.....	8	3.3
.040.....	12	2.8	.0375.....	8	3.3
.040.....	10	2.5	.038.....	7	3.7
Average.....		V=2.1	.040.....	11	2.3
			.040.....	7	3.6
			Average.....		V=2.7
P., D. AND CO.			B. W. AND CO.		
0.0375.....	17	1.6	0.03.....	13	2.6
.0375.....	14	1.9	.03.....	16	2.2
.040.....	13	1.9	.03.....	12	2.7
.040.....	14	1.8	.035.....	15?	1.9
.040.....	14	1.8	.035.....	10	2.8
.0425.....	11	2.1	.035.....	9	3.2
.0425.....	10	2.4	.04.....	8	3.1
.0425.....	11	2.1	.04.....	7½	3.3
.045.....	10	2.2	Average.....		V=2.7
.045.....	11	2.0			
.045.....	8	2.8	S. AND D.		
.045.....	9	2.5	0.036.....	16	1.8
Average.....		V=2.1	.038.....	10	2.6
			.038.....	12	2.2
LLOYD BROS.			.040.....	11	2.3
0.035.....	15	1.9	.040.....	10	2.2
.0375.....	13	2.1	.045.....	9	2.5
.040.....	12	2.1	.045.....	8	2.8
.040.....	10	2.5	.045.....	7	2.8
.0425.....	12	1.9	Average.....		V=2.4
.045.....	8	2.9			
.045.....	9	2.4			
Average.....		V=2.3			

^a Calculated as of fluid extract strength.

Digitalone No. 1. Frog, weight 41 grams, injected with 0.5 c. c. per gram body weight. Five hours later heart rate was 16, weak contraction but dilating well.

Digitalone No. 2. Frog, weight 40 grams, injected with 0.5 c. c. per gram body weight. Five hours later heart still beating, rate 17, contractions weak, but dilating fairly well.

Digitalone No. 3. Frog, weight 39 grams, injected with 0.5 c. c. per gram body weight. Ventricle stopped in fifty-seven minutes; auricles beat two hours longer.

TABLE VI.—*Determination of toxic dose for Rana pipiens. Focke method—drug injected into leg lymph sacs—Continued.*

SUMMARY.

Preparation.	V (value).
Mulford No. 1.....	3.8
N. B. and Co.....	2.9
B. W. and Co.....	2.7
H. B. and W.....	2.7
S. and D.....	2.4
Lloyd Bros.....	2.3
P., D. and Co.....	2.1
Merrell.....	2.1
Digitalone 1, 2, 3.....

PERFUSION OF FROG'S HEART.

The perfusion experiments upon excised frogs' hearts were carried out by tying a cannula in the left trunk of the aorta and a second in the posterior vena cava near the heart. The isolated heart was perfused under constant pressure with Ringer's solution to which digitalis in tincture strength was added so as to make a 1 per cent solution. The time was noted until systolic stoppage of the heart appeared and the figures recorded indicate the number of minutes the heart continued beating after the introduction of the drug. The results obtained by this method are recorded in Table VII.

TABLE VII.—*Determination of the time required to stop the isolated heart of Rana pipiens with Ringer's solution to which digitalis had been added to make the solution of 1 per cent tincture strength.*

	Minutes.		Minutes.
Mulford No. 2.....	23	N. B. and Co.....	17
	26		18
	21		28
	21		19
	18		20
	22		16
	14		21
	15		
	15	Average.....	20
	16		
	21	H. B. and W.....	17
	18		15
Average.....	19		21
			23
Merrell.....	31		16
	35		18
	17	Average.....	18
	35		
	37	P., D. and Co.....	20
	34		32
	21		12
	35		33
Average.....	31		44
			26
B. W. and Co.....	19		12
	30		16
	29		19
	21		22
	26		26
	17	Average.....	24
	18		
Average.....	23	S. and D.....	29
			27
Lloyd Bros.....	66		25
	71		32
	54		26
	48		32
	46		29
Average.....	57		20
		Average.....	28
Digitalone No. 3.....	53		
	47		
	78		
	65		
	97		
	72		
Average.....	69		

SUMMARY.

Preparation.	Minutes.
H. B. and W.....	18
Mulford No. 2.....	19
N. B. and Co.....	20
B. W. and Co.....	23
P., D. and Co.....	24
S. and D.....	28
Merrell.....	31
Lloyd Bros.....	57
Digitalone No. 3.....	69

THE BLOOD PRESSURE METHOD OF ASSAY.

The blood-pressure method, included in a third group by our classification, was carried out in the ordinary manner, cats being used as experimental animals. They were anæsthetized with chloretone, 0.4 gram per kilogram body weight, dissolved in a small amount of alcohol (2 c. c. to 1 gram chloretone) diluted with a little water and given by the stomach after the method of Edmunds and Cushny.^a The comparison of the various preparations of digitalis is made upon the percentage of rise in blood pressure which followed the injection of 1 c. c. of the various solutions when diluted with normal salt solution to tincture strength. Only one preparation could be used upon one animal, and from two to four animals were used for each preparation in order that the average of the results obtained might more accurately represent the value of the drug used. The results of these experiments, which are tabulated in Table III, page 37, are summarized in the following table:

TABLE VIII.—*Summary of results obtained on blood pressure.—Average per cent rise after 1 cubic centimeter doses intravenously.*

Preparation.	Per cent increase.
N. B. and Co.	99
Mulford No. 2.	64
Digitalone No. 2.	55
B. W. and Co.	51
P., D. and Co.	37
S. and D.	35
H. B. and W.	33
Merrell.	26
Digitalone No. 3.	26
Lloyd Bros.	24
Digitalone No. 1.	1—23

¹ Fall.

To enable a comparison to be made of the relative strengths of the different digitalis preparations as obtained by the different methods of assay employed, we have grouped all the findings in Table IX.

TABLE IX.—*Summary of results obtained by the several methods for the standardization of digitalis preparations.*

LETHAL-DOSE METHODS.

Mice.	Guinea pigs.	Frogs (twelve-hour).	Cats.
Mulford No. 1. <i>mg.</i> 4	B. W. and Co. <i>mg.</i> 0.35	B. W. and Co. <i>c. c.</i> 0.015	B. W. and Co. <i>mg.</i> 158
B. W. and Co. 4	H. B. and W. 5	Mulford No. 2.020	P., D. and Co. 171
Merrell. 6	Merrell. 6	S. and D.027	N. B. and Co. 192
H. B. and W. 7	Mulford No. 1. 7	P., D. and Co.029	Mulford No. 2. 195
P., D. and Co. 8	P., D. and Co. 7		H. B. and W. 219
N. B. and Co. 9	N. B. and Co. 9		S. and D. 242
S. and D. 9	S. and D. 9		Merrell. 252
Digitalone No. 1. 22	Lloyd Bros. 9		Digitalone No. 3. 280
Lloyd Bros. 24	Digitalone No. 1. 5.0		Lloyd Bros. 438
	Digitalone No. 3. ^b 1.5		Digitalone No. 2. 550

^a Edmunds and Cushny, Laboratory Guide in Experimental Pharmacology, p. 12.^b Lived.

TABLE IX.—*Summary of results obtained by the several methods for the standardization of digitalis preparations—Continued.*

FROG-HEART METHODS.

One hour.		"Focke."		Perfusion.	
	<i>c. c</i>		<i>V.</i>		<i>min.</i>
Mulford No. 1.....	0.012	Mulford No. 2.....	3.8	H. B. and W.....	18
Mulford No. 2.....	.016	N. B. and Co.....	2.9	Mulford No. 2.....	19
B. W. and Co.....	.020	B. W. and Co.....	2.7	N. B. and Co.....	20
P., D. and Co.....	.021	H. B. and W.....	2.7	B. W. and Co.....	23
N. B. and Co.....	.022	S. and D.....	2.4	P., D. and Co.....	24
Merrell.....	.024	Lloyd Bros.....	2.3	S. and D.....	28
H. B. and W.....	.025	P., D. and Co.....	2.1	Merrell.....	31
S. and D.....	.027	Merrell.....	2.1	Lloyd Bros.....	57
Lloyd Bros.....	.030			Digitalone No. 3.....	69
Digitalone No. 3.....	.040				

BLOOD-PRESSURE METHOD.

	<i>Per cent.</i>		<i>Per cent.</i>
N. B. and Co.....	99	H. B. and W.....	33
Mulford No. 2.....	64	Merrell.....	26
Digitalone No. 2.....	55	Digitalone No. 3.....	26
B. W. and Co.....	51	Lloyd Bros.....	24
P., D. and Co.....	37	Digitalone No. 1.....	a—23
S. and D.....	35		

a Fall.

Table X has been arranged from Table IX to show in a numerical way the relative position the preparations experimented with occupy. The figures represent the relative position each preparation holds with reference to its activity as determined by the various methods of assay. In case two preparations showed the same strength (as for instance the Concentrated tincture, B. W. and Co. and Digitol, Mulford on mice) they have been given equal ranking.

TABLE X.—*Rearrangement of Table IX to show the relative activity of the following preparations as determined by the various methods of assay.*

Preparations.	Lethal dose methods.				Frog heart methods.			Blood Pressure.
	Mice.	Guinea pigs.	Twelve hour.	Cats.	One hour.	"Focke."	Perfusion.	Per cent increase.
B. W. and Co.....	1	1	(a)	1	2	3	4	4
Mulford.....	1	4		4	1	1	2	2
Merrell.....	3	3		7	5	7	7	8
H. B. and W.....	4	2		5	6	4	1	7
P., D. and Co.....	5	4		2	3	7	5	5
N. B. and Co.....	6	6		3	4	2	3	1
S. and D.....	6	6		6	7	5	6	6
Digitalone No. 1.....	8	9						
Lloyd Bros.....	9	8		9	8	6	8	10
Digitalone No. 3.....		(b)		8	9		9	8
Digitalone No. 2.....				10				5

a The results obtained by the twelve-hour method are not included because too few experiments were carried out according to it to give the preparations their proper rank.

b Lived.

DISCUSSION OF METHODS OF ASSAY.

A superficial examination of the tables giving the summary of the results obtained would seem to indicate the practical worthlessness of the biological assay of digitalis preparations by the methods now in vogue. This is especially emphasized by a comparison of Digital and the Concentrated tincture made by Burroughs, Wellcome & Co. These give comparative values as follows:

	Mice, toxic dose.	Guinea pigs. toxic dose.	Frogs, one hour.
	<i>mgm.</i>	<i>mgm.</i>	<i>c. c.</i>
Digital No. 1.....	4.0	0.70	0.012
Concentrated tincture.....	4.0	.35	.020

Here are two preparations which according to the first test are of the same strength; by a second test one is half the strength of the other, and by a third method exactly the reverse relation is found. No explanation can be suggested for the results obtained on mice and guinea pigs; there was no possibility of a mistake, as the results were confirmed on numerous animals as the tables show, and with different solutions made up on different days. A closer examination of the table shows that these results are certainly exceptional, the vast majority being more uniform, as, for example, the two preparations named are shown by most of the methods to be the strongest of any of the specimens examined. Also comparing the four U. S. Pharmacopœia fluid extracts made by Hance Brothers & White, Parke, Davis & Co., Nelson, Baker & Co., and Sharpe & Dohme, these were found by several of the methods to be of very nearly the same strength, differing not more than 25 per cent. Also the Digitalone preparations and Lloyd's Specific Medicine appear at the bottom of the list in almost every table showing by every method their comparative weakness.

There appears thus to be some slight uniformity in the results obtained by the different methods. This is indeed far from close, but this fact is not surprising when the factors concerned in the different methods of assay are considered. In the first place it could hardly be expected that animals differing so widely as cats and frogs, mice and guinea pigs would react exactly alike to the different preparations. The cause of death is not the same in the mice and guinea pigs as in the frogs and the cats under the conditions of our experiments. With frogs the action is always one upon the heart; also in the cats we maintained artificial respiration so that the figures obtained there indicate a cardiac action. On both mice and guinea pigs, however, the cause of death in probably every case is not due

to an action upon the heart but upon the medulla. In every animal we examined we found the heart beating after the respiration had stopped, and it continued to beat as long as artificial respiration was maintained. It would not then be at all surprising if two solutions which showed a certain relationship when the cardiac action was concerned should show an entirely different relation when the central nervous system was the point of attack. One solution might be very weak in its action upon the heart and yet contain decomposition products of digitalis whose typical action is upon the medulla and it would therefore appear unduly strong when judged by such a standard. For this reason *we think that methods which employ as a standard the minimum lethal dose obtained upon the higher animals are not applicable to the physiological assay of the digitalis series.*

It is possible that still further complications would arise in using such methods in that on certain animals of the same species some would die from the cardiac effect and others from the medullary action. In some of the cats, for instance, distinct respiratory movements were seen after the heart had stopped and the blood pressure had fallen to zero; in others the respiration stopped first. As stated earlier, to avoid complications of this sort, in our experiments on cats we always employed artificial respiration.

Comparing the toxic doses obtained upon cats and frogs (twelve-hour method) we have in both cases a cardiac action and three of the four preparations show relatively the same activity; the Parke, Davis & Co. Fluid Extract alone being an exception. But that an exception should occur is not to be wondered at when the differences between the heart of the frog and that of the cat are considered. Also in the blood pressure experiments on the cat we have to do with substances acting upon the vessel walls as well as upon the heart and this necessarily introduces another factor as some of the digitalis active principles act more strongly upon vessel walls than others, and in two preparations of digitalis the active substances may not be present in the same relative amounts.

The "Focke" and the "one-hour" methods upon frogs might be thought to give a closer agreement, but here (aside from the difficulties connected with Focke's method which have been discussed) we have to deal with the question of ease of absorption. As has been pointed out by some earlier writers, in those methods in which the time element is very limited, a weak preparation with easily absorbable constituents would appear stronger than a strong preparation with constituents which are absorbed with difficulty. It would seem that such an objection might be of importance in the "Focke" method, where from seven to twenty minutes only are allowed. As to whether it would play a part in the "one-hour" method is of course possible

but not very probable, when it is remembered with what rapidity the action appears when digitoxin in solution is injected.

The reason that the "frog's heart perfusion" method does not agree with the other frog methods is possibly due partly to the more uniform character of the solution of the poison in which the heart is bathed and also to the resinous precipitate which forms and falls to the bottom of the perfusion vessel and which no doubt contains some of the active constituents.

From this short critical review of the different methods for standardization it can easily be seen why no two methods of assay could be expected to give exactly the same relative values to a series of digitalis preparations, especially when they are made according to radically different methods, such differences as exist, for instance, between a "Fat free" tincture and a "Specific medicine." The agreement is much closer when the preparations are made according to the same formula as we have in the case of the official fluid extracts.

It would appear then most desirable if manufacturing houses could agree upon a certain method to be used which would insure the different preparations upon the market under the same name having the same potency. As to the choice of such a method difficulties would arise, but certainly none which would appear insurmountable. The method chosen should be as simple as possible, and above all *an action upon the circulation should be taken as a standard of comparison rather than an action upon the nervous system.* Judged by these rules, some of the methods now in use are not suitable for the purpose.

First, we have the toxic action upon the higher animals, which should not be used for the reasons given earlier. The technical difficulties of the Focke method, together with the question of completeness of absorption, exclude it. The perfusion of the frog's heart is also excluded for reasons mentioned and also because it requires more skill to carry it out, and even then the variations in results are very great. The blood-pressure method upon cats and dogs commends itself on account of the close relation it sustains to the use of the drug in clinical practice. The objections consist in the difficulty of procuring these animals at times and also the necessity of carrying out repeated experiments to confirm the results, which a study of our tables show will vary very greatly. A dose of a certain preparation which in one animal may cause a rise of perhaps 70 or 80 per cent in blood pressure may in others not raise it more than one-quarter as much, but probably repeated tests will give reliable results.

The toxic dose can also be obtained at the same time by using artificial respiration, but, as our tables show, there need be no agreement between the two, and it therefore seems superfluous. This leaves, then, the two frog methods—the "twelve-hour" toxic method and the

"one-hour" method. As between them it is impossible to choose with any degree of accuracy. With the "one-hour" method we have the advantage of there being no delay, it being possible to assay a preparation in three or four hours, and it probably takes fewer frogs than the "twelve-hour" method. On the other hand, with the latter method, although taking four or five days to complete the assay, it need not interfere with other work, as the frogs can be injected late in the afternoon and examined the next morning. Between these two methods, then, as far as can be judged, it is largely a question of personal preference and convenience, at least in the light of our present knowledge. Our results do not show that they give the same relative values to the four specimens examined by them, and as to which is correct it is impossible to say. They do roughly agree in that Burroughs, Wellcome & Co.'s Concentrated Tincture and Digital are both stronger than the two fluid extracts of Parke, Davis & Co. and Sharpe & Dohme. This relationship is confirmed by every other method which we employed, excepting that using the toxic dose as found on cats. It would not seem, therefore, to be unreasonable to suppose that such a relationship would probably exist in man.

As to the desirability of manufacturing houses standardizing their preparations belonging to the digitalis series there can be no question.

It is true that the official preparations examined herewith are approximately of the same strength, but the crude drug obtained in another year may represent altogether a different toxicity to that employed in the manufacture of these preparations, and the only way at present to avoid like variations in the tinctures and fluid extracts is to standardize them by physiological methods. It is not claimed that such methods are infallible. They certainly are not, as we have shown; but, as we have also shown, most of the apparent discrepancies are due to the fact that actions upon quite different physiological functions are taken as a measure of activity. Such discrepancies can be avoided by the adoption of one or the other of these frog methods, and if it is thought necessary the results obtained can be confirmed by blood-pressure experiments upon cats or, preferably, dogs.

We believe the chief point to be kept in mind is that, in spite of annoying individual discrepancies, there is a general agreement between the various methods. This agreement, too, is much more complete in the case of those methods in which the toxic effect is due to an action upon the heart. A preparation found weak by one method appears weak by all methods, and one showing marked activity by one shows the same result in all.

The second part of the research, that which is concerned with the different preparations, requires little to be added to that already given in the tables. We have arranged, however, the different preparations in the order of their relative strengths as determined

by the results obtained by all the methods of assay. Such a list is found in Table XI. This is prepared from Table X by adding together the numbers denoting the relative position of each preparation and dividing the sum by the number of assay methods used. Naturally the quotients thus found will stand in inverse ratio with the strength of the preparation.

In this table the results obtained by the "twelve-hour" method on frogs were not used, as only four preparations were assayed according to it, so that no true ranking in relation to the results obtained by the other methods could be found.

TABLE XI.

Preparation.	Sum of ratings.	Number of assays.	Final result.
Mulford.....	15	7	2.14
B., W. and Co.....	16	7	2.28
N., B. and Co.....	25	7	3.57
H. B. and W.....	29	7	4.14
P., D. and Co.....	31	7	4.43
Merrell.....	40	7	5.71
S. and D.....	42	7	6.00
Lloyd Bros.....	58	7	8.28
Digitalone No. 3.....	34	4	8.50
Digitalone Nos. 1 and 2.....			

Such a table as this we think, on the whole, represents very fairly the relative strengths of the different preparations examined. It represents the final conclusion drawn from a very large series of experiments, and on that account may be considered fairly accurate.

There are only four preparations which would appear to require special mention. These are the normal tincture of digitalis made by William S. Merrell Chemical Company, of Cincinnati; digitalone made by Parke, Davis & Co., of Detroit; the specific medicine, digitalis made by Lloyd Bros., of Cincinnati, and tincture digitol made by H. K. Mulford & Co., of Philadelphia. Two bottles of digitol were examined. By the one-hour method on frogs they did not show the same strength, one requiring 0.012 c. c. to produce systolic stoppage of the heart in one hour and the other 0.016 c. c. (Table IX.) This preparation, as mentioned earlier, is "assayed, tested physiologically" and standardized to contain 0.025 gram digitoxin in 100 c. c.

The purified normal tincture of Merrell is said to be "a standardized neutral tincture of prime digitalis leaves freed from the irritating fats and oils." In our tables the dose of this preparation was always calculated upon the basis of fluid extract strength, which is not correct, as normal tinctures are said to be made from fresh leaves which are put into alcohol. Later the alcohol is expressed and by evaporation 1 kilo of the solution is made equivalent to 1 kilo of leaves. It is thus considerably weaker than a fluid extract on account of the moisture content of the fresh plant. But even calculated in this

way it compares fairly well with the fluid extracts, especially by the "toxic" methods. The maximum dose recommended is about 3 minims, or about the same as for a fluid extract.

The "Specific Medicine" digitalis, made by Lloyd Bros., of Cincinnati, offered some difficulties on account of its high alcohol content (80 per cent absolute). If this was evaporated off, a gummy resinous mass was left which was very hard to mix with water in such a way as to give uniform dosage. In many cases to avoid this trouble the solution was merely exposed in any open vessel at room temperature until part of the alcohol had evaporated, and the residue was then mixed with the water to get the desired dilution. The solutions thus obtained were always thoroughly shaken to insure a uniform distribution of the precipitate. In one method, namely, the perfusion of the frog's heart, it is not possible to get the full action of the drug, as the precipitate which forms when the drug is added to the Ringer's solution settles to the bottom of the bottle containing the perfusion fluid and only the soluble portion reaches the heart. It is for this reason that the drug appears so much weaker by this method than by the other methods in which the animal receives the entire drug. The results of our experiments show that the preparation is uniformly weaker than the pharmacopœial fluid extracts. According to the label its strength is 480 grains to the fluid ounce.

In the advertising literature of this firm the effect upon the system of the "Specific Medicines" is said to be about double that of ordinary fluid extracts and the dose should not be more than one-half the usual dose of fluid extracts. The dose recommended on the bottle is from one-third minim to 1 minim *every hour*, which is certainly not less than that of a pharmacopœial fluid extract. In general, its strength would appear to be about the same as the fluid extracts; it certainly is not stronger.

Three bottles of digitalone were examined. This is said to be an aseptic nonalcoholic, permanent solution of digitalis of the same strength as the U. S. Pharmacopœia tincture. Bottles Nos. 1 and 2 were not essentially different in the character of the preparation contained. In both cases it possessed a peculiar, somewhat aromatic odor, not exactly unpleasant, but somewhat sour. The fluids were both a dark brown and contained a rather heavy precipitate. Bottle No. 3, the odor was not as unpleasant, and somewhat suggested chloretone. The preparation was slightly lighter in color than an orange yellow, and contained a fairly abundant, fine white, flaky precipitate.

Their relative physiological activity can be most clearly illustrated by three experiments upon frogs carried out under similar conditions, the hearts being exposed and the drug being injected in relatively the same size doses.

DIGITALONE No. 1.

August 17, 1908. Frog, 41 grams:

- 11.25. Heart rate 27 in twenty seconds.
- 11.29. Heart rate 28 in twenty seconds.
- 11.30. Injected 2.05 c. c. digitalone No. 1; 0.05 c. c. per gram body weight.
- 11.42. Heart rate 18 in twenty seconds.
- 11.50. Heart rate 16 in twenty seconds.
- 12.01. Heart rate 16 in twenty seconds.
- 12.30. Heart rate 17 in twenty seconds.
- 2.15. Heart rate 16 in twenty seconds; heart weak.
- 4.30. Heart rate 16 in twenty seconds; dilates poorly and very weak contraction.

DIGITALONE No. 2.

August 17, 1908. Frog, 40 grams:

- 11.00. Heart rate 30 in twenty seconds.
- 11.05. Heart rate 37 in twenty seconds.
- 11.05. Injected 2 c. c. digitalone No. 2.
- 11.10. Heart rate 15 (?) in thirty seconds; irregular peristaltic contractions.
- 11.18. Heart rate 16 in twenty seconds; normal contractions.
- 11.27. Heart rate 16 in twenty seconds.
- 11.41. Heart rate 16 in twenty seconds; systole weak.
- 11.50. Heart rate 16 in twenty seconds.
- 12.30. Heart rate 15 in twenty seconds.
- 2.15. Heart rate 17 in twenty seconds; weak.
- 4.15. Heart rate 17 in twenty seconds; weak, dilating fairly well.

DIGITALONE No. 3.

August 17, 1908. Frog, 39 grams:

- 10.55. Heart rate 26 in twenty seconds.
- 11.01. Heart rate 26 in twenty seconds.
- 11.02. Injected 1.95 c. c. digitalone No. 3.
- 11.06. Heart rate 11 in twenty seconds; systole prolonged.
- 11.12. Heart rate 10 in twenty seconds.
- 11.16. Heart rate 16 in twenty seconds; dilates little.
- 11.40. Heart rate 7 in twenty seconds, little dilatation.
- 11.59. Ventricle in systole; auricles, rate 7 in twenty seconds.
- 2.30. Auricle stopped; ventricle in systole.

Specimens Nos. 1 and 2 showed no digitalis action whatever, while No. 3 was quite weak.

To kill mice Digitalone No. 1 required from two and one-half to five times the dose that any other preparation examined required excepting Lloyd's "Specific Medicine, digitalis." On guinea pigs 2 milligrams per kilogram body weight caused death, but as pointed out earlier it was a question whether this was due to the digitalis per se or to the effect of an injection under the skin of 12.5 c. c. of fluid containing chloretone and possibly digitalis decomposition products. The animal became comatose at once, showing no characteristic digitalis symptoms. Preparation No. 2, tested by the twelve-hour method on frogs, did not cause death in doses as high as 0.07 c. c. per gram body weight, while the preparations made according to the

other methods caused death in doses from one-quarter to one-half as large. In the one-hour method Digitalone No. 2, in doses four times as large as were given of the weakest and ten times as large as the strongest of the other (excepting Digitalone) preparations, failed to call forth systolic standstill of the heart. Digitalone No. 3 seemed to be fairly active. By the one-hour method on frogs it was from one-third to two-thirds as strong as the other preparations. Focke's method was not very successful on account of the extremely large dose which would have required so much concentration on the water bath to bring it to a volume small enough to inject into the lymph sacs. This specimen failed to kill guinea pigs when used in doses twice as large as the average preparation required. Injected into rabbits Digitalone No. 1, instead of raising the blood pressure, lowered it 23 per cent, the curve resembling that given by the nitrite series. Digitalone No. 3 raised the blood pressure 26 per cent.

An interesting fact in connection with the value of the blood-pressure methods of assay is that Digitalone No. 2, which was shown by the exposed frog's heart to be almost devoid of digitalis action, caused a rise of 55 per cent in the blood pressure of two cats. It might be that some other substances are present (perhaps decomposition products) which, possessing no cardiac effect, yet act on the vasomotor system, probably upon the center. In specimen No. 1 other changes in the solution must have occurred, as at each injection a fall in blood pressure followed. The important conclusion to be drawn from these experiments is that Digitalone is not invariably a permanent solution. Those preparations which have decomposed are not only devoid of any digitalis action, but are distinctly harmful. A preparation which evidently had not deteriorated completely seemed to be about half the strength of an official tincture.

LIST OF HYGIENIC LABORATORY BULLETINS OF THE PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.

The Hygienic Laboratory was established in New York, at the Marine Hospital on Staten Island, August, 1887. It was transferred to Washington, with quarters in the Butler Building, June 11, 1891, and a new laboratory building, located in Washington, was authorized by act of Congress, March 3, 1901.

The following *bulletins* [Bulls. Nos. 1-7, 1900 to 1902, Hyg. Lab., U. S. Mar.-Hosp. Serv., Wash.] have been issued:

*No. 1.—Preliminary note on the viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 2.—Formalin disinfection of baggage without apparatus. By M. J. Rosenau.

*No. 3.—Sulphur dioxid as a germicidal agent. By H. D. Geddings.

*No. 4.—Viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 5.—An investigation of a pathogenic microbe (*B. typhi murium* Danyz) applied to the destruction of rats. By M. J. Rosenau.

*No. 6.—Disinfection against mosquitoes with formaldehyd and sulphur dioxid. By M. J. Rosenau.

No. 7.—Laboratory technique: Ring test for indol, by S. B. Grubbs and Edward Francis; Collodium sacs, by S. B. Grubbs and Edward Francis; Microphotography with simple apparatus, by H. B. Parker.

By act of Congress approved July 1, 1902, the name of the "United States Marine-Hospital Service" was changed to the "Public Health and Marine-Hospital Service of the United States," and three new divisions were added to the Hygienic Laboratory.

Since the change of name of the Service the bulletins of the Hygienic Laboratory have been continued in the same numerical order, as follows:

*No. 8.—Laboratory course in pathology and bacteriology. By M. J. Rosenau. (Revised edition, March, 1904.)

*No. 9.—Presence of tetanus in commercial gelatin. By John F. Anderson.

No. 10.—Report upon the prevalence and geographic distribution of hookworm disease (uncinariasis or anchylostomiasis) in the United States. By Ch. Wardell Stiles.

*No. 11.—An experimental investigation of *Trypanosoma lewisi*. By Edward Francis.

*No. 12.—The bacteriological impurities of vaccine virus; an experimental study. By M. J. Rosenau.

*No. 13.—A statistical study of the intestinal parasites of 500 white male patients at the United States Government Hospital for the Insane; by Philip E. Garrison, Brayton H. Ransom, and Earle C. Stevenson. A parasitic roundworm (*Agamomermis culicis* n. g., n. sp.) in American mosquitoes (*Culex sollicitans*); by Ch. Wardell Stiles. The type species of the cestode genus *Hymenolepis*; by Ch. Wardell Stiles.

No. 14.—Spotted fever (tick fever) of the Rocky Mountains; a new disease. By John F. Anderson.

No. 15.—Inefficiency of ferrous sulphate as an antiseptic and germicide. By Allan J. McLaughlin.

*No. 16.—The antiseptic and germicidal properties of glycerin. By M. J. Rosenau.

*No. 17.—Illustrated key to the trematode parasites of man. By Ch. Wardell Stiles.

*No. 18.—An account of the tapeworms of the genus *Hymenolepis* parasitic in man, including reports of several new cases of the dwarf tapeworm (*H. nana*) in the United States. By Brayton H. Ransom.

*No. 19.—A method for inoculating animals with precise amounts. By M. J. Rosenau.

*No. 20.—A zoological investigation into the cause, transmission, and source of Rocky Mountain "spotted fever." By Ch. Wardell Stiles.

No. 21.—The immunity unit for standardizing diphtheria antitoxin (based on Ehrlich's normal serum). Official standard prepared under the act approved July 1, 1902. By M. J. Rosenau.

*No. 22.—Chloride of zinc as a deodorant, antiseptic, and germicide. By T. B. McClintic.

*No. 23.—Changes in the Pharmacopœia of the United States of America. Eighth Decennial Revision. By Reid Hunt and Murray Galt Motter.

No. 24.—The International Code of Zoological Nomenclature as applied to medicine. By Ch. Wardell Stiles.

No. 25.—Illustrated key to the cestode parasites of man. By Ch. Wardell Stiles.

No. 26.—On the stability of the oxidases and their conduct toward various reagents. The conduct of phenolphthalein in the animal organism. A test for saccharin, and a simple method of distinguishing between cumarin and vanillin. The toxicity of ozone and other oxidizing agents to lipase. The influence of chemical constitution on the lipolytic hydrolysis of ethereal salts. By J. H. Kastle.

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*No. 28.—A statistical study of the prevalence of intestinal worms in man. By Ch. Wardell Stiles and Philip E. Garrison.

*No. 29.—A study of the cause of sudden death following the injection of horse serum. By M. J. Rosenau and John F. Anderson.

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No. 31.—Variations in the peroxidase activity of the blood in health and disease. By Joseph H. Kastle and Harold L. Amoss.

No. 32.—A stomach lesion in guinea pigs caused by diphtheria toxine and its bearing upon experimental gastric ulcer. By M. J. Rosenau and John F. Anderson.

No. 33.—Studies in experimental alcoholism. By Reid Hunt.

No. 34.—I. *Agamofilaria georgiana* n. sp., an apparently new roundworm parasite from the ankle of a negress. II. The zoological characters of the roundworm genus *Filaria* Mueller, 1787. III. Three new American cases of infection of man with horse-hair worms (species *Paragordius varius*), with summary of all cases reported to date. By Ch. Wardell Stiles.

*No. 35.—Report on the origin and prevalence of typhoid fever in the District of Columbia. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle. (Including articles contributed by Ch. Wardell Stiles, Joseph Goldberger, and A. M. Stimson.)

No. 36.—Further studies upon hypersusceptibility and immunity. By M. J. Rosenau and John F. Anderson.

No. 37.—Index-catalogue of medical and veterinary zoology. Subjects: Trematoda and trematode diseases. By Ch. Wardell Stiles and Albert Hassall.

No. 38.—The influence of antitoxin upon post-diphtheritic paralysis. By M. J. Rosenau and John F. Anderson.

No. 39.—The anticeptic and germicidal properties of solutions of formaldehyde and their action upon toxines. By John F. Anderson.

No. 40.—1. The occurrence of a proliferating cestode larva (*Sparganum proliferum*) in man in Florida, by Ch. Wardell Stiles. 2. A reexamination of the type specimen of *Filaria restiformis* Leidy, 1880=*Agamomermis restiformis*, by Ch. Wardell Stiles. 3. Observations on two new parasitic trematode worms: *Homalogaster philippinensis*

n. sp., *Agamodistomum nanus* n. sp., by Ch. Wardell Stiles and Joseph Goldberger.
 4. A reexamination of the original specimen of *Tænia saginata abietina* (Weinland, 1858), by Ch. Wardell Stiles and Joseph Goldberger.

*No. 41.—Milk and its relation to the public health. By various authors.

No. 42.—The thermal death points of pathogenic micro-organisms in milk. By M. J. Rosenau.

No. 43.—The standardization of tetanus antitoxin (an American unit established under authority of the act of July 1, 1902). By M. J. Rosenau and John F. Anderson.

No. 44.—Report No. 2 on the origin and prevalence of typhoid fever in the District of Columbia, 1907. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle.

No. 45.—Further studies upon anaphylaxis. By M. J. Rosenau and John F. Anderson.

No. 46.—*Hepatozoon perniciosum* (n. g. n. sp.); a haemogregarine pathogenic for white rats; with a description of the sexual cycle in the intermediate host, a mite (*Lelaps echidninus*). By W. W. Miller.

No. 47.—Studies on Thyroid.—I. The Relation of Iodine to the Physiological Activity of Thyroid Preparations. By Reid Hunt and Atherton Seidell.

No. 48.—The Physiological Standardization of Digitalis. By Charles Wallis Edmunds and Worth Hale.

In citing these bulletins, beginning with No. 8, bibliographers and authors are requested to adopt the following abbreviations: Bull. No. —, Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv., Wash., pp. —.

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TREASURY DEPARTMENT
Public Health and Marine-Hospital Service of the United States

HYGIENIC LABORATORY.—BULLETIN No. 49

MARCH, 1909

DIGEST OF COMMENTS
ON THE
PHARMACOPŒIA OF THE UNITED STATES
OF AMERICA

[EIGHTH DECENNIAL REVISION]

FOR THE PERIOD ENDING DECEMBER 31

1905

BY
MURRAY GALT MOTTER
AND
MARTIN I. WILBERT



WASHINGTON
GOVERNMENT PRINTING OFFICE

1909

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WALTER WYMAN, *Surgeon-General,*
United States Public Health and Marine-Hospital Service.

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TABLE OF CONTENTS.

	Page.
Preface	7
List of literature reviewed.....	13
1. Title abbreviations—Journals	13
2. Title abbreviations—Pharmacopœias	17
I. General comments	19
1. General principles to be followed in revising the pharmacopœia, extract from the abstract of proceedings, U. S. P. C., 1900..	19
1. Scope	19
2. Doses	20
3. Nomenclature	20
4. Assay processes	20
5. Purity and strength	20
6. General formulæ	21
7. Weights and measures	21
8. Supplement	21
9. Limitations	21
10. Synonyms	21
11. Precedents	21
12. Medicine dropper	21
13. Powdered drugs	22
2. Scope:	22
1. Time of publication	22
2. Scope of the Pharmacopœia	24
3. Synthetics	25
4. New remedies	27
5. Doses	28
6. Nomenclature	29
7. Chemical formulas	30
8. Assay processes	30
9. Purity and strength	32
10. Standardization	33
11. Changes in strength	33
12. General formulas	33
13. Weights and measures	34
14. Additions and deletions	34
15. Drops and droppers	35
16. Powdered drugs	35
3. Analytical data:	36
1. Adulterations	36
2. Analytical methods and results	37
3. Reagents	37
4. Atomic weights	38
5. Indicators	39
6. Ash determinations	40

I. General comments—Continued.	Page.
3. Analytical data—Continued.	
7. Specific gravity	41
8. Solubilities	41
9. Boiling-point determinations	42
10. Melting-point determinations	42
11. Thermometric tables	43
12. Polarization and refraction	43
13. Filters	44
14. Oxidation	44
15. Color standards	44
16. Alkalinity of glass	44
17. Tests	45
4. Biologic remedies	52
5. Vegetable drugs	54
1. Constituents	55
2. Microscopical descriptions	57
6. Pharmaceutical preparations	58
1. Decomposition	58
2. Incompatibility	58
3. Galenicals	59
4. Percolation	60
5. Production of extracts and tinctures	61
6. Sterilization	61
7. Forms of administration	62
II. International standards	64
1. International conference for the unification of pharmacopœial formulæ for potent medicaments (Brussels Conference)	64
1. Projet d'Arrangement	64
2. Comparative table showing degrees of compliance therewith	69
3. Drops	77
4. Comments on the U. S. P. VIII relative to requirements of	77
2. Foreign pharmacopœias	77
1. Dutch	77
2. Spanish	78
3. British	80
4. Italian	80
5. Danish	81
6. Swiss	81
Spanish edition of the U. S. P. VIII	81
Pharmacopœial history	82
III. Comments on official articles	83

PREFACE.

The reorganization of the Marine-Hospital Service in 1871, under the direction of a supervising surgeon-general, evidenced the advisability of extending the work of this service so as to provide for much needed supervision of varied interests relating to the public health.

Of the many activities that have been developed by the service in this connection, few are of more wide-spread importance to the welfare of the public at large, or more intimately connected with the medical efficiency of the service itself, than an active participation and interest in the revision of the Pharmacopœia of the United States. This fact was early recognized and the service has been regularly represented at each decennial meeting of the Pharmacopœial Revision Convention held since its reorganization as a bureau in 1871, and several of the representatives of the Marine-Hospital Service have served as members of the revision committee. The Marine-Hospital Service was also among the first of the government services to adopt the pharmacopœia as the standard for its medical supplies and to require that drugs and medicines conform strictly with these official requirements.

With the change of name of the service to the Public Health and Marine-Hospital Service, this need for cooperation in improving the scientific accuracy of the pharmacopœia has become even more evident. The requirements have in a measure been met by the introduction of a division of scientific research, the establishment in the Hygienic Laboratory of a division of pharmacology devoted to the scientific investigation of drugs as they relate to the public health, particularly with reference to their potency and pharmacopœial purity, and the distinct authorization to undertake the supervision and practical control of certain important medicinal products, such as sera and vaccines.

As evidence that the nature of this cooperation is appreciated, it may be pointed out that the description given for diphtheria antitoxin in Bulletin No. 21 of the Hygienic Laboratory was included in the U. S. P., VIII, without change, has proven to be generally acceptable, and provides that "the standard of strength expressed in antitoxic power should be that approved or established by the

United States Public Health and Marine-Hospital Service." (U. S. P., VIII, p. 393.)

The publication of the U. S. P., VIII, in July, 1905, followed as it was by the passage of the food and drugs act of June 30, 1906, has served to attract attention to the contents and the provisions of the former in a way that was quite unexpected, even by the members of the committee of revision of the Pharmacopœia of the United States.

This, at the time unforeseen, development has served the twofold purpose of interesting a much larger number of individuals in the pharmacopœia, and of eliciting a much greater number of comments and criticisms on its contents than has ever before been forthcoming.

It has long been appreciated that proper recognition should be given to all forms of comments and criticisms in the development of the pharmacopœia, and for more than a quarter of a century the committee of revision of the pharmacopœia, or the chairman of that committee, has been instrumental in collecting and considering the criticisms offered in current medical and pharmaceutical literature.

So far as is known the origin of compilations of this kind is to be attributed to the late Charles Rice, who, as chairman of the committee of revision of the Pharmacopœia of the United States in 1883, began to collect notes and abstracts taken from the medical and pharmaceutical literature of this country and Europe with the view of forming a digest of criticisms for the use of future members of the revision committee of the U. S. P.

In the introduction to Part 1 of this Digest of Criticisms, Charles Rice points out that it would be necessary for the revision committee of the pharmacopœia to have access to a comprehensive compilation of the criticisms on the pharmacopœia and the substances related to it, if they were expected to reflect accurately the practices of the time and the requirements of medical practitioners in the resulting book.

He also points out the difficulties that beset the compiler of material of this kind and considered himself as particularly fortunate in being able to secure the services of the late Hans M. Wilder, of Philadelphia, to devote all of his time to the compilation of the material for the first five parts of the six so far published of the "Digest of Criticisms on the United States Pharmacopœia."

These digests of criticisms were published by the committee of revision of the Pharmacopœia of the United States for gratuitous distribution to such persons as were particularly interested in the revision of the pharmacopœia or who might be able to assist in the perfecting of that book. Because of the widespread and growing interest in the U. S. P., VIII, and because of the official connection of the Public Health and Marine-Hospital Service with the United States Pharmacopœial Convention, the board of trustees of the latter

organization requested the cooperation of the Surgeon-General of the Public Health and Marine-Hospital Service of the United States in the compilation and publication of a "Digest of Comments" bearing on the articles official in the U. S. P., VIII.

It is in compliance with this request that the following material is presented for the consideration of the members of the committee of revision of the Pharmacopœia of the United States, the officers of this service, and of such other persons as have manifested or may manifest an interest in making the pharmacopœia and are anxious or willing to contribute to the further development and perfecting of that book.

The compilers of the following abstracts have endeavored to gather together and to present in an impartial way, and without the addition of critical remarks, all comments on the Pharmacopœia of the United States and the several articles contained therein that were available in the literature reviewed. Being a compilation of material presented by other authors, the compilers are in no way responsible for the opinions expressed, though it should be remembered that it is not always practicable, or even possible, to suggest in a brief paragraph the content or the exact import or trend of a lengthy, comprehensive article, so that, for practical purposes, this digest should be considered rather in the nature of a series of suggestions—an elaborated index—while for working details it will be advisable to consult the original article, so as to avoid possible, though unintentional, misinterpretations of the author's purpose. It should be remembered, too, that while many of the ideas and opinions here cited may appear to be positive and based on good authority, still, they are not authoritative, and that, until they have been critically examined and incorporated in the pharmacopœia itself, they can not in any way be considered as being official.

It will be remembered that following the enactment of the food and drugs act, June 30, 1906, it was found desirable to make a number of changes in the requirements for drugs and chemicals; these changes will be considered in due course, but, for the present, practically all of the references bearing more directly on these several changes have been omitted as being no longer of interest or necessary.

For the presentation of the material it was necessary to decide on some definite method of procedure, and in view of the varied nature of the literature reviewed and the difficulties met with in securing access to the several publications, it was decided to compile the material chronologically, so as to present the available comments in proper sequence.

Almost without exception the present bulletin deals only with the literature of the latter half of 1905, representing the period from the publication of the U. S. P., VIII, to December 31, 1905, though it

should be remembered that at least some of this literature is recorded in journals and periodical publications that can not themselves be accurately classed as belonging to the literature of 1905; thus many of the reviews consulted, while they deal with the literature for 1905, themselves belong to the literature of the year in which they were published.

Many of the ideas and opinions herein presented are manifestly impracticable, but are nevertheless suggestive, and the compilers have not considered themselves justified in ignoring or eliminating them. Old and previously discarded ideas are frequently revived as new discoveries. Such alleged discoveries should be considered with an added degree of conservatism, as the very fact of their having been previously advanced would suggest that they have evident shortcomings, in some respect at least.

As noted before, it would be manifestly impracticable to abstract at length all of the really important contributions bearing on the material contained in the U. S. P., and it has frequently been found necessary to refer to even the more important articles in an extremely brief way. This brevity, it is hoped, will have the advantage of suggesting the need of consulting the original article itself.

So far as it has been practicable the original article has been consulted and is directly referred to. In the many instances where this has not been possible or practicable an effort has been made to quote the most readily accessible reference that is sufficiently comprehensive to be of value as indicating the intent as well as the content of the original article. For the medical literature the compilers have confined themselves largely to several well-known medical journals, and to a review of the *Index Medicus* for such additional references as might be of service in indicating the use or the possibilities of official substances. In this connection it may be of interest to point out that several homœopathic and eclectic medical journals have been reviewed, primarily to record such suggestions as they might have to offer, and secondarily to demonstrate the evident widespread use of official articles by the followers of the several sectarian schools of medicine.

In the main the arrangement of the material presented closely follows that originated by the late Charles Rice, though it was thought inadvisable to follow the abbreviations used by him or to confine the review to the journals included in the earlier numbers of the "*Digest of Criticisms*."

For the abbreviations of the journal titles it was thought advisable to follow very largely the abbreviations of titles of medical periodicals employed in the *Index Catalogue* of the library of the Surgeon-General's Office and in the *Index Medicus*. These abbreviations, while far from satisfactory, are the most generally used, certainly the

best known, in this country, and until some definite and generally accepted understanding relating to abbreviations for the titles of current journals is agreed to, might well be even more generally adhered to.

In attempting to consult a representative number of journals and periodical publications it was found that for various reasons the representative libraries of this country are particularly deficient in current pharmaceutical literature. To overcome this deficiency an effort is now being made to develop, in connection with the compilation of abstracts, a representative reference library of current pharmaceutical and chemical literature.

The proceedings of the several state pharmaceutical associations are particularly difficult to obtain, and the officials of the Public Health and Marine-Hospital Service are to be congratulated on having been able to secure the cooperation of a number of the officers of these several organizations and obtain from them a fairly representative collection of the current numbers of their proceedings. As yet this collection is far from complete, and the Chief of the Division of Pharmacology of the Hygienic Laboratory, Washington, will be pleased to hear from anyone who is willing to contribute toward the completion of the files of pharmaceutical or chemical journals or of state pharmaceutical association proceedings.

In conclusion, the compilers wish to express their own appreciation of the shortcomings of the compilation as presented, and beg to assure the members of the medical and pharmaceutical professions that comments on the method of presenting the material will be welcome, and that, so far as they are able, they will endeavor to profit by any suggestions that may be offered for improving the style or the contents of future bulletins.

M. I. W.
M. G. M.

DIVISION OF PHARMACOLOGY,
HYGIENIC LABORATORY,
March, 1909.

LIST OF THE LITERATURE REVIEWED.

1. TITLE ABBREVIATIONS—JOURNALS.

- Am. Chem. J.—American Chemical Journal, Baltimore, 1905, v. 34.
 Am. Druggist, N. Y.—American Druggist, New York, 1905, v. 47.
 Am. J. Med. Sc.—American Journal of the Medical Sciences, Philadelphia, 1905, v. 129, 130.
 Am. J. Pharm.—American Journal of Pharmacy, Philadelphia, 1905, v. 77.
 Am. Therapist, N. Y.—American Therapist, New York, 1905, v. 14.
 Am. Vet. Rev.—American Veterinary Review, New York, 1905, v. 14.
 Analyst, London, 1905, v. 30.
 Ann. d. Chem., Leipz.—Justus Liebig's Annalen der Chemie, Leipzig, 1905, v. 341, 342, 343.
 Ann. de chim. analyt., Paris.—Annales de chimie analytique, Paris, 1905, v. 10.
 Ann. de pharm., Louvain.—Annales de Pharmacie, Louvain, 1905, v. 11.
 Ann. Bot. Lond.—Annals of Botany, London, 1905, v. 19.
 Ann. Rep., U. S. Dep't. Agric.—Annual Report of the U. S. Department of Agriculture for 1905.
 Apothecary, Boston, 1905, v. 17.
 Apoth. Ztg.—Apotheker Zeitung, Berlin, 1905, v. 20.
 Arb. a. d. kais. Gesundheitsamte, Berlin.—Arbeiten aus dem kaiserlichen Gesundheitsamte, Berlin, 1905, v. 23.
 Arb. a. d. pharm. Inst. d. Univ. Berlin.—Arbeiten aus dem pharmazeutischen Institut der Universität Berlin, for 1905 (1906), v. 3.
 Arch. d. Pharm., Berlin.—Archiv der Pharmazie, Berlin, 1905, v. 243.
 Arch. f. Pharm. og Chem., Copenhagen.—Archiv for Pharmacie og Chemie, Copenhagen, 1905, v. 12.
 Arch. f. expt. Path. u. Pharmacol., Leipz.—Archiv für experimentelle Pathologie und Pharmacologie, Leipzig, 1905, v. 52, 53, 54.
 Arch. internat. de Pharmacod. et de Thérap.—Archives internationales de Pharmacodynamie et de Thérapie, Brussels and Paris, 1905, v. 14.
 Arch. di. farm. sper., Rome.—Archivio di farmacologia sperimentale, Rome, 1905, v. 4.
 Australasian J. Pharm.—Australasian Journal of Pharmacy, Melbourne, 1905, v. 20.
 Beitr. z. chem. Phys. u. Path.—Beiträge zur chemischen Physiologie und Pathologie, Braunschweig (Brunswick), 1905-6, v. 7.
 Ber. d. deutsch. chem. Gesellsch., Berlin.—Berichte der deutschen chemischen Gesellschaft, Berlin, 1905, v. 39.
 Ber. d. phar. Gesellsch., Berlin.—Berichte der pharmaceutischen Gesellschaft, Berlin, 1905, v. 15.
 Biochem. Centralbl., Leipz.—Biochemisches Centralblatt, Leipzig, 1905-6, v. 4.
 Bol. d. Ministerio de Agric., Buenos Aires.—Boletín del Ministerio de Agricultura, Buenos Aires, 1905, v. 3.
 Boll. Chim. Farm., Milan.—Bolettino chimico farmaceutico, Milan, 1905, v. 44.
 Bot. Gaz., Chicago.—Botanical Gazette, Chicago, 1905, v. 40.
 Bot. Centralbl., Cassel.—Botanisches Centralblatt, Cassel, for 1905, v. 99, 100.

- Bot. Jahrb. Engler, Leipz.—Botanische Jahrbücher, Engler, Leipzig, 1905, v. 36.
- Brit. & Col. Druggist, Lond.—British and Colonial Druggist, London, 1905, v. 48.
- Brit. Food J., Lond.—British Food Journal, London, 1905, v. 7.
- Bull. Bur. Chem., U. S. Dep't Agric.—Bulletin of the Bureau of Chemistry, U. S. Department of Agriculture, 1905.
- Bull. Bur. Plant Ind., U. S. Dep't Agric.—Bulletin of the Bureau of Plant Industry, U. S. Department of Agriculture, 1905.
- Bull. Dep't Agric., Jamaica.—Bulletin of the Department of Agriculture, Jamaica, 1905, v. 3.
- Bull. Hyg. Lab., U. S. P. H. & M. H. S.—Bulletin of the Hygienic Laboratory of the Public Health and Marine-Hospital Service, 1905.
- Bull. de Pharm. du Sud-Est, Montpellier.—Bulletin de pharmacie du Sud-Est, Montpellier, 1905, v. 10.
- Bull. Pharm., Detroit.—Bulletin of Pharmacy, Detroit, 1905, v. 19.
- Bull. des Sc. Pharmacol., Paris.—Bulletin des Sciences Pharmacologiques, Paris, 1905, v. 12.
- Bull. Soc. Roy. de Pharm. de Bruxelles.—Bulletin de la Société de Pharmacie de Bruxelles (Brussels), 1905, v. 49.
- Bull. de la Soc. sc. et méd. de l'ouest.—Bulletin de la société scientifique et médicale de l'ouest, Rennes, 1905, v. 14.
- Bull. Soc. de pharm. de Bordeaux.—Bulletin des travaux de la Société de Pharmacie de Bordeaux, 1905, v. 45.
- Bull. Torrey Bot. Club.—Bulletin of the Torrey Botanical Club, Chicago, 1905, v. 32.
- Canad. Druggist, Toronto.—Canadian Druggist, Toronto, 1905, v. 17.
- Canad. Pharm. J. Toronto.—Canadian Pharmaceutical Journal, Toronto, 1905, v. 39.
- Chem. Eng., Phila.—Chemical Engineer, Philadelphia, 1905-6, v. 3.
- Chem. News, Lond.—Chemical News, London, 1905, v. 91, 92.
- Chem. Ztg., Cöthen.—Chemiker-Zeitung, Cöthen, 1905, v. 29.
- Chem. Repert.—Chemisch Technisches Repertorium, Cöthen, 1905.
- Chem. Centralbl.—Chemisches Centralblatt, Berlin, 1905, v. 76.
- Chem. & Drug., Lond.—Chemist and Druggist, London, 1905, v. 67.
- Chron. Med. Mex., Mexico.—Chronica Medica Mexicana, Mexico, 1905, v. 8.
- Circ. & Agric. J., Roy. Bot. Gard., Ceylon.—Circular and Agricultural Journal, Royal Botanical Garden, Ceylon, 1905, v. 3.
- Compt.-rend. Acad. d. sc., Paris.—Comptes rendus, hebdomadaires des séances de l'Académie des sciences, Paris, 1905, v. 141.
- Compt.-rend. Soc. de biol. Paris.—Comptes Rendus des séances et mémoires de la Société de biologie, Paris, 1905, v. 75.
- Dental Cosmos, Philadelphia, 1905, v. 47.
- Deutsch-Amer. Apoth. Ztg., N. Y.—Deutsch-Amerikanische Apotheker Zeitung, New York, 1905, v. 26.
- Drug. Circ. & Chem. Gaz., N. Y.—Druggists Circular and Chemists Gazette, New York, 1905, v. 49.
- Drug Topics, N. Y., 1905, v. 20.
- Eclectic Med. J.—Eclectic Medical Journal, Cincinnati, 1905, v. 65.
- Exp. Sta. Rec.—Experiment Station Record, U. S. Department of Agriculture, 1905-06, v. 16, 17.
- Geschäfts-Ber. von Caesar & Loretz, in Halle a. S. 1905.
- Hahneman. Month., Phila.—Hahnemannian Monthly, Philadelphia, 1905, v. 40.
- Handels-Ber. Gehe & Co.—Handels-Bericht, Gehe & Co., Dresden, 1905.
- Index Medicus, 1905, v. 3.

- Jahresb. f. Tier Chem., Wiesbaden.—Jahresbericht über Tier Chemie, Wiesbaden, 1905, v. 35.
- J. d'Agric. Trop., Paris.—Journal d'Agriculture Tropicale, Paris, 1905, v. 5.
- J. d. Pharm. d'Anvers.—Journal de Pharmacie d'Anvers (Antwerp), 1905, v. 61.
- J. d. Pharm. von Elsass-Lothr.—Journal der Pharmacie von Elsass-Lothringen, Mülhausen, 1905, v. 32.
- J. de pharm. et de chim., Paris.—Journal de Pharmacie et de Chimie., Paris, 1905, v. 22.
- J. Am. Chem. Soc.—Journal of the American Chemical Society, Easton, 1905, v. 27.
- J. Am. M. Ass.—Journal of the American Medical Association, Chicago, 1905, v. 45.
- J. Biol. Chem., N. Y.—Journal of Biological Chemistry, New York, 1905-6, v. 1.
- J. Chem. Soc., Lond.—Journal of the Chemical Society, London, 1905, v. 87, 88.
- J. Pharm. Soc., Japan.—Journal of the Pharmaceutical Society, Japan, 1905.
- J. Soc. Chem. Ind., Lond.—Journal of the Society of Chemical Industry, London, 1905, v. 24.
- Just's Bot. Jahresb.—Just's Botanischer Jahresbericht, Berlin, for 1905, v. 33.
- Med. News, N. Y.—Medical News, New York, 1905, v. 87.
- Merck's Archives, N. Y. 1905, v. 7.
- Merck's Report, N. Y., 1905, v. 14.
- Meyer Bro. Druggist, St. Louis, 1905, v. 26.
- Midland Druggist, Columbus, 1905, v. 6.
- Nat. Druggist, St. Louis.—National Druggist, St. Louis, 1905, v. 35.
- New Idea, Detroit, 1905, v. 27.
- Nouv. Rem., Paris.—Nouveaux Remèdes, Paris, 1905, v. 21.
- Oesterr. chem. Ztg.—Oesterreichische chemiker Zeitung, Wien, 1905, v. 8.
- Paint, Oil and Drug Rep., N. Y.—Paint, Oil and Drug Reporter, New York, 1905, v. 68.
- Pflanzer (Der) Tanga, 1905, v. 1.
- Pharm. Era, N. Y.—Pharmaceutical Era, N. Y., 1905, v. 34.
- Pharm. J. Lond.—Pharmaceutical Journal London, 1905, v. 21.
- Pharm. Rev.—Pharmaceutical Review, Milwaukee, 1905, v. 23.
- Pharm. Post. Wien.—Pharmazeutische Post, Wien, 1905, v. 38.
- Pharm. Praxis.—Pharmazeutische Praxis, Stuttgart, 1905, v. 4.
- Pharm. Weekblad.—Pharmaceutisch Weekblad voor Nederland, Amsterdam, 1905, v. 42.
- Pharm. Ztg.—Pharmazeutische Zeitung, Berlin, 1905, v. 50.
- Pharm. Zentralh.—Pharmazeutische Zentralhalle, Dresden, 1905, v. 46.
- Proc. Am. Pharm. Ass.—Proceedings of the American Pharmaceutical Association, 1905, v. 53.
- Proc. Am. Philosoph. Soc.—Proceedings of the American Philosophical Society, Philadelphia, 1905, v. 43.
- Proceedings of state pharmaceutical associations:
- Proc. Alabama Pharm. Ass., 1905.
 - Proc. Arkansas Pharm. Ass., 1905.
 - Proc. Connecticut Pharm. Ass., 1905.
 - Proc. Georgia Pharm. Ass., 1905.
 - Proc. Illinois Pharm. Ass., 1905.
 - Proc. Indiana Pharm. Ass., 1905.
 - Proc. Iowa Pharm. Ass., 1905.
 - Proc. Kansas Pharm. Ass., 1905.
 - Proc. Kentucky Pharm. Ass., 1905.

Proceedings of state pharmaceutical associations—Continued.

- Proc. Louisiana Pharm. Ass., 1905.
 Proc. Maine Pharm. Ass., 1905.
 Proc. Maryland Pharm. Ass., 1905.
 Proc. Massachusetts Pharm. Ass., 1905.
 Proc. Michigan Pharm. Ass., 1905.
 Proc. Minnesota Pharm. Ass., 1905.
 Proc. Mississippi Pharm. Ass., 1905.
 Proc. Missouri Pharm. Ass., 1905.
 Proc. Nebraska Pharm. Ass., 1905.
 Proc. New Hampshire Pharm. Ass., 1905.
 Proc. New Jersey Pharm. Ass., 1905.
 Proc. New York Pharm. Ass., 1905.
 Proc. North Carolina Pharm. Ass., 1905.
 Proc. Ohio Pharm. Ass., 1905.
 Proc. Pennsylvania Pharm. Ass., 1905.
 Proc. South Carolina Pharm. Ass., 1905.
 Proc. Tennessee Pharm. Ass., 1905.
 Proc. Texas Pharm. Ass., 1905.
 Proc. Vermont Pharm. Ass., 1905.
 Proc. Wisconsin Pharm. Ass., 1905.
 Proc. Off. Agric. Chem. 22d Ann. Conv.—Proceedings of the 22d Annual Convention, Official Agricultural Chemists, Washington, 1906.
 Proc. Roy. Soc., Lond.—Proceedings, Royal Society of London, 1905, v. 76.
 Répert. de pharm., Paris.—Répertoire de Pharmacie, Paris, 1905, v. 17.
 Rep. Missouri Bot. Gard., St. Louis.—Report, 17th annual, of the Missouri Botanical Garden for 1905, St. Louis, 1906.
 Rev. Med. de Bogota.—Revista Medica de Bogota, 1905, v. 25, 26.
 Rev. Med. de Chile.—Revista Médica de Chile, 1905, v. 33.
 Riedel's Berichte, Berlin, 1905.
 Riedel's Mentor, Berlin, 1905.
 Schweiz. Wchnschr. f. Chem. u. Pharm.—Schweizerische Wochenschrift für Chemie und Pharmacie, 1905, v. 43.
 Sc. Am. Suppl.—Scientific American Supplement, New York, 1905, v. 60.
 Semi-Ann. Rep., Schimmel & Co.—Semi-Annual Report of Schimmel & Co., Miltitz, 1905.
 Spatula, Boston, 1905, v. 11.
 Storrs Station Rep., 17th Ann., 1905.
 Suedd. Apoth. Ztg.—Sueddeutsche Apotheker Zeitung., 1905, v. 45.
 Svensk. farm. Tidskr.—Svensk Farmaceutisk Tidskrift, Stockholm, 1905, v. 9.
 Tech. Quart., Boston.—Technology Quarterly, Boston, 1905, v. 19.
 Therap. Gaz.—Therapeutic Gazette, Detroit, 1905, v. 29.
 Therap. Monatsh.—Therapeutische Monatshefte, Berlin, 1905, v. 19.
 Therap. d. Gegenw.—Therapie der Gegenwart, Berlin, 1905, v. 46.
 Trans. Am. Inst. Homœop.—Transactions of American Institute of Homœopathy, 1905, v. 51.
 Trans. Am. Therap. Soc.—Transactions of the American Therapeutic Society, 1905.
 Tropenpflanzer (Der) Berlin, 1905, v. 9.
 Western Druggist, Chicago, 1905, v. 27.
 Year Book of Pharmacy, London, 1905.
 Ztschr. f. anal. Chem.—Zeitschrift für analytische Chemie, Wiesbaden, 1905, v. 44.
 Ztschr. f. angew. Chem.—Zeitschrift für angewandte Chemie, Berlin, 1905, v. 18.

- Ztschr. f. anorg. Chem.—Zeitschrift für anorganische Chemie, Hamburg, 1905, v. 43, 44, 45.
- Ztschr. f. expt. Path. u. Therap.—Zeitschrift für experimentelle Pathologie und Therapie, Berlin, 1905, v. 1.
- Ztschr. f. oeffentl. Chem.—Zeitschrift für oeffentliche Chemie, 1905, v. 11.
- Ztschr. f. Unters. Nahr. u. Genussm.—Zeitschrift für Untersuchung der Nahrungs und Genussmittel, Berlin, 1905, v. 9, 10.

TITLE ABBREVIATIONS—PHARMACOPŒIAS.

- Ph. Austr. VIII.—Pharmacopoea Austriaca, editio octava, 1906.
- Ph. Belg. III.—Pharmacopœa Belgica, editio tertia, 1906.
- Ph. Brit. IV.—British Pharmacopoea, 1898.
- Ph. Dan.—Pharmacopœa Danica.
- Ph. Fr. (1908).—Codex Medicamentarius Gallicus. Pharmacopée Française. 1908.
- Ph. Germ. IV.—Deutsches Arzneibuch, editio quarta, 1900.
- Ph. Helv. IV.—Pharmacopoea Helvetica, editio quarta, 1907.
- Ph. Hisp. VII.—Farmacopea oficial Española, séptima edición, 1905.
- Ph. Hung.—Pharmacopoea Hungarica, editio secunda, 1888.
- Ph. Japon.—Pharmacopoea Japonica, editio secunda, 1891.
- Ph. Ital.—Farmacopoea ufficiale del regno d'Italia, 1903.
- Ph. Ndl. IV.—Pharmacopoea Nederlandica, editio quarta, 1905.
- Ph. Norv.—Pharmacopoea Norwegica, editio tertia, 1895.
- Ph. Port.—Pharmacopoea Portugueza, 1876.
- Ph. Rom.—Pharmacopoea Romana, editio tertia, 1893.
- Ph. Russ.—Pharmacopoea Rossica, editio quarta, 1893.
- Ph. Svec.—Pharmacopoea Svecica, editio septima, 1879. Supplem.
- U. S. P., VIII.—Pharmacopœia of the United States of America, 8th Dec. Rev., 1905.

(Modified from Hirsch, Bruno, 1902, Universal Pharmakopœe.)

DIGEST OF COMMENTS ON THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA.

EIGHTH DECENNIAL REVISION.

I. GENERAL COMMENTS.

To facilitate reference and to avoid unnecessary repetition in connection with a number of the questions involved, the following "general principles to be followed in revising the pharmacopœia" are here reproduced from the "abstract of the proceedings of the national convention of 1900 for revising the Pharmacopœia of the United States."

These principles were, in the main, embodied in the draft of a plan for revising the pharmacopœia of 1890 presented by the committee of revision created by the convention of 1890. They are important in connection with a digest of the comments on the pharmacopœia in that they indicate the lines along which the U. S. P., VIII, was revised, and tend to suggest the modifications that should be embodied in the draft of a plan for revising the U. S. P., VIII, to be presented and discussed at the forthcoming convention in 1910.

1. GENERAL PRINCIPLES TO BE FOLLOWED IN REVISING THE PHARMACOPŒIA.

In accordance with the instructions of the convention of 1890, the committee of revision created by this body herewith presents a draft of a plan for revising the pharmacopœia of 1890.

1. SCOPE OF THE PHARMACOPŒIA.

The committee of revision is authorized to admit into the pharmacopœia any product of nature of known origin; also any synthetized product of definite composition which is in common use by the medical profession, the identity, purity, or strength of which can be determined. No compound or mixture shall be introduced if the composition or mode of manufacture thereof be kept secret, or if it be controlled by unlimited proprietary or patent rights.

2. DOSES.

After each pharmacopœial article (drug, chemical, or preparation) which is used or likely to be used internally or hypodermically the committee is instructed to state the average approximate (but neither a minimum nor a maximum) dose for adults, and, where deemed advisable, also for children. The metric system to be used, and the approximate equivalent ordinary weights or measures inserted in parentheses.

It is to be distinctly understood that neither this convention nor the committee of revision created by it intends to have these doses regarded as obligatory on the physician or as forbidding him to exceed them whenever in his judgment this seems advisable. The committee is directed to make a distinct declaration to this effect in some prominent place in the new pharmacopœia.

3. NOMENCLATURE.

It is recommended that changes in the titles of articles at present official be made only for the purpose of insuring greater accuracy or safety in dispensing. In the case of newly admitted articles it is recommended that such titles be chosen as are in harmony with general usage and convenient for prescribing; but in the case of chemicals of a definite composition a scientific name should be given at least as a synonym.

4. ASSAY PROCESSES.

The committee is instructed to append assay processes to as many of the potent drugs and preparations made therefrom as may be found possible, provided that the processes of assay are reasonably simple (both as to methods and apparatus required) and lead to fairly uniform results in different hands. As regards the products of such assays, tests of identity and purity should be added wherever feasible. Physiological tests for determining strength should not be introduced by the committee.

5. PURITY AND STRENGTH OF PHARMACOPŒIAL ARTICLES.

The committee is instructed to revise as carefully as possible the limits of purity and strength of the pharmacopœial chemicals and preparations for which limiting tests are given. While no concession should be made toward a diminution of medicinal value, allowance should be made for unavoidable, innocuous impurities or variations due to the particular source or mode of preparation, or to the keeping qualities of the several articles. In the case of natural products the limits of admissible impurities should be placed high enough to exclude any that would not be accepted by other countries.

Regarding the strength of diluted acids, tinctures, and galenical preparations in general, it is recommended that the committee keep

in view the desirability of at least a gradual approach upon mutual concessions toward uniformity with similar preparations of other pharmacopœias, particularly in the case of potent remedies which are in general use among civilized nations.

6. GENERAL FORMULÆ.

It is recommended that general formulæ be introduced, as far as the particular nature of the several drugs will permit, for fluid extracts, tinctures, and such other preparations as are made by identical processes, and that the general formula to be followed in each case be merely indicated by reference.

7. WEIGHTS AND MEASURES.

The committee is instructed to retain the metric system of weights and measures as adopted in the seventh decennial revision.

8. SUPPLEMENT.

That the committee on revision be authorized to prepare a supplement to the pharmacopœia at any time they may deem such action desirable.

The delegates from the Ohio State Pharmaceutical Association offered the following suggestions:

9. LIMITATIONS.

It is recommended that every article in the United States Pharmacopœia that has no medicinal value and is used solely for commercial or technical purposes be discarded from the next issue of the United States Pharmacopœia.

10. SYNONYMS.

It is recommended that every common name and English title of articles used in the present United States Pharmacopœia that is synonymous for both the medicinal and commercial drug be either discarded or modified so as to leave no doubt as to what is wanted.

11. PRECEDENTS.

In all matters not specially provided for in these "general principles" the rules established for previous revisions, if there are any, should be followed.

Several additional resolutions are recorded as having been offered and discussed, but not adopted.

12. MEDICINE DROPPER.

At the fourth session Dr. Wm. H. Seaman offered the following:

It is recommended that an official medicine dropper have its delivery end 3 millimetres in external diameter, and adapted to deliver 20 drops of distilled water to a gramme at 15° C.

This was referred without recommendation to the Committee on Revision.

13. POWDERED DRUGS.

Dr. H. H. Rusby moved that the Committee on Revision be requested to consider the advisability of treating the subject of powdered drugs in the text of the pharmacopœia. The motion was adopted.

2. SCOPE.

Remington, J. P., in discussing the report of the A. Ph. A. committee on the U. S. P., commends the "Digest of Criticisms," started by the late Dr. Charles Rice, as being an excellent medium for presenting the consensus of opinions on the pharmacopœia and an important factor in the improvement of the pharmacopœia itself:

Commenting on the criticisms offered, he says:

We welcome criticisms, and true pharmacists will tender them in a spirit of helpfulness, and every member of the committee will do what he can to make the book as perfect as possible.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 253-256.

Lyons, A. B., discusses the inequalities necessarily found in a book of this kind and suggests that in future the preface to the pharmacopœia contain a statement of the reasons for making certain changes "in the physician's book of standards."—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 256-263.

Martin, H. Newell, joins most heartily in the chorus of praise, but regrets the paucity of preparations in both the American and British pharmacopœias. Believes that the number of these preparations should be greatly augmented.—*Ibid.*, p. 352.

1. TIME OF PUBLICATION

Whelpley, H. M., in a communication as secretary of the convention, discusses the publication of the U. S. P. and the difficulties that were encountered.—*Pharm. J. Lond.*, 1905, v. 21, p. 273. (Also other medical and drug journals.)

The editor gives a comprehensive account of "Revising the Pharmacopœia—The workers and their methods of work."—*Am. Druggist*, N. Y., 1905, v. 47, p. 99.

The editor in commenting on the time of publication says:

The pharmacopœia of 1890 was published in August, 1893, and became official January 1, 1894—four and a fraction months later. The pharmacopœia of 1900 was published in July, 1905, and became official September 1, 1905—one and a fraction months later.—*Drug, Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 313.

Remington, J. P., in discussing the time when the new pharmacopœia became official, explains that unexpected delays necessitated the change.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 354.

Leffman, Henry, maintains that the work should have been published in 1900 and that the delay of five years gives it a lack of comprehensiveness.—*Med. News*, N. Y., 1905, v. 87, p. 1276.

Remington, J. P., says:

The book was delayed because the United States has been unable, until within the last three months, to form a standard for diphtheria antitoxin.—*Proc. Penna. Pharm. Ass.*, 1905, p. 74.

"Gnomon" understands that the delay in publication has been caused by prolonged negotiations having for their object the finding of a firm of publishers which should offer the best terms.—*Pharm. J.*, Lond. 1905, v. 21, p. 70.

Caldwell, Paul, says:

Enough time has not been allowed for the circulation of the book among druggists to allow them to be prepared for the official change.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 307.

Wilbert, M. I., points out that the time required for the revision could be reduced if the book were thoroughly criticised before the meeting of the national convention.—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 370.

Williams, S. W., says that unless an interval of six months or more can be provided for between the date on which the pharmacopœia can be freely bought and the date on which it becomes "official," something in the nature of a "prospectus" should be presented to the trade sufficiently in advance to allow manufacturers and others to adapt themselves to the required changes.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 308.

The editor records the difficulty of securing copies of the pharmacopœia during July, August, and September.—*Ibid.*, p. 341.

Editorial note on letters received explaining why pharmacopœias can not be supplied.—*Ibid.*, p. 414.

The editor discusses the relation between the number of pharmacopœias sold and the number of drug stores in the country.—*Ibid.*, p. 304.

The editor suggests that publicity be given to the work of revision and thus increase the interest in the book and secure for it a far larger measure of support than it has ever had from either pharmacists or physicians.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 442.

The editor discusses the several communications that have appeared relative to the publication of commentaries and other publications bearing on the U. S. P., VIII.—*Chem. & Drug.*, Lond., 1905, v. 67, p. 545.

Cowley, R. C., deprecates the publication of upwards of 75 pages of matter relating largely to the individual members of the several committees and the members of the national convention.—*Brit. & Col. Drug.*, Lond., 1905, v. 48, p. 382.

MacEwan, Peter, suggests that in future the U. S. P. and B. P. be published in quinquennial intervals, the B. P. in 1910, the U. S. P. in 1915, and so on.—*Am. Druggist*, N. Y., 1905, v. 47, p. 95.

2. SCOPE OF THE PHARMACOPŒIA.

The editor says that "the book shows that in it there is much to commend and but little to condemn," and that the committee of revision deserves the congratulations of physicians and pharmacists for the excellent standard that has been prepared.—*Pharm. Era*, N. Y., 1905, v. 34, p. 3.

The editor points out that "there is an air of conservatism about the book and its contents which suggests that the compilers are not devoid of caution."—*Chem. & Drug.*, Lond., 1905, v. 67, p. 51.

The editor suggests that the very excellence of the pharmacopœia is a source of fear. "In a work of this kind the most important consideration is its adaptability to existing conditions," and the question arises, Is the book perfectly adapted to the requirements of American pharmacists as they are now?—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 263.

Wilbert, M. I., deplotes the recognition of articles having a purely local demand.—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 356.

Upsher-Smith points out that "it does not follow that articles added are necessarily of value, nor that others dismissed are necessarily worthless." He also suggests that physicians compile a book of select remedies. He does not appreciate the need for a book with pharmaceutical, physical, and pharmacognostical details.—*Pharm. J.*, Lond., 1905, v. 21, p. 885.

The editor calls attention to the generally acknowledged fact that the pharmacopœia is the one book that pharmacists have thought they could best get along without.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 263.

The editor asserts that "it has been a standing reproach to the medical profession in general that they have taken so little interest in this important work." He further expresses the opinion that this is fast becoming a matter of history, and that the time is not far distant when the pharmacopœia will be a living part of every practitioner's armamentarium.—*Med. News*, N. Y., 1905, v. 87, p. 361.

"B. H. C.," Pennsylvania, suggests that it would be better to have but one standard and everything in that one book fully covered, both as to scope and requirements.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 393.

Wetterstroem, Theo. D., suggests that the use of alcohol, glycerin, borax, benzoin, and hypophosphorous acid should suffice to indicate that foreign admixture should not always be construed to be adulteration, particularly when it can be shown that the intent to deceive or defraud is lacking.—*Ibid.*, p. 312.

Lyons, A. B., says that "a criticism that seems quite just is one on the needless omission of the various preparations into the composition

of which each article enters."—Proc. Am. Pharm. Ass., 1905, v. 53, p. 260.

Wilbert, M. I., calls attention to "the main objects which a physician usually has, or would have, for consulting a pharmacopœia," as defined by the late Charles Rice, and points out that in some very important respects the U. S. P., VIII, does not comply with these requirements.—Am. J. Pharm., Phila., 1905, v. 77, p. 355.

A series of articles entitled "The Pharmacopœia and the Physician" includes a general review of the history of the Pharmacopœia of the United States of America and its evolution, with some reference to its scope and content.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 1869 ff.

Bell, J. W. (St. Paul Med. J., August, 1905), expresses the hope that with the new pharmacopœia and other factors now at work we may see the weak link in medicine, therapeutics, so strengthened in the near future as to commend itself alike to the public and to the skeptic within the profession.—Abstr. *Ibid.*, p. 812.

Marshall, C. R., would like to see more work done specially for a pharmacopœia and under the auspices of its authorities, and less dependence on outside and sporadic help. Everything in a pharmacopœia should be put to the test by men well qualified and specially appointed for the task, even if the work may have been done by others before.—Pharm. J. Lond., 1905, v. 21, p. 716.

Lyons, A. B., says the National Formulary is a work that should be prepared with as much care as the pharmacopœia. "Elegant pharmacy" has no place in the pharmacopœia, and unless these preparations are provided by some generally recognized authority physicians will be deprived of their use or driven to the manufacturers for such remedies as they are willing to prescribe.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 262.

In an editorial review of the Spanish Pharmacopœia it is pointed out that the revisers of that book have taken the position where the manufactured article is now universally and currently sold in a satisfactory state, the process may be omitted; but where the laboratory preparation is simple and advantageous the formula should be given. In every case the leading characteristics and reagents for detecting adulterations should be given.—Brit. & Col. Druggist, Lond., 1905, v. 48, p. 480.

Hinrichs, Carl G., discusses at some length the chemistry of the U. S. P., VIII.—Am. J. Pharm., Phila., 1905, v. 77, p. 503.

3. SYNTHETICS.

Hallberg, C. S. N., points out that "the committee compromised by admitting such products for which the patent on the process or product, or both, expired or will expire before the end of the present

decade (1910), provided that by such expiration the trade name would also become free."—J. Am. M. Ass., Chicago, 1905, v. 45, p. 110.

Williams, S. W., in commenting on the admission of synthetics calls attention to the fact that the whole question is much involved and will be made a matter for international adjustment.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 308.

Hinrichs, Carl G., points out that the committee on revision has followed in the wake of the British, Germans, and French in introducing synthetics, and that it would indeed be folly to refuse these agencies a place in the U. S. P. He deprecates the omission of the trade names, at least as synonyms.—Am. J. Pharm., Phila., 1905, v. 77, p. 505.

"Gnomon," taking a suggestion from the preface of the new U. S. P., urges the publication of a list giving date of patent, date of expiration, and proprietary rights, if any, in the name used.—Pharm. J., Lond., 1905, v. 21, p. 388.

Wilbert, M. I., calls attention to the intricate nature of the problems involved in the official recognition of synthetics and compares the trade names of several of the newly admitted synthetic remedies with the official titles given them in the U. S. P., VIII, the Ph. Brit., IV, and the Ph. Germ., IV.—Am. J. Pharm., Phila., 1905, v. 77, p. 356.

Gane, E. H., in the address as chairman of the section on scientific papers of the A. Ph. A., suggests that we are going too fast for the business pharmacist and assuming too much interest on his part in scientific studies. He also points out the desirability of cooperating with the council on pharmacy and chemistry of the American Medical Association so as to control the unnecessary proliferation of synthetics and new remedies.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 174–179.

The editor, in commenting on the absence of well-known synthetics, says:

It is due to the pharmacists of the Union that these articles should appear under their common names.—Canad. Pharm. J., Toronto, v. 39, p. 213.

The editor wonders whether pharmacists and physicians will ever get to know the old familiar synthetics under their new names, and, at this late day, use these names in place of the customary ones.—Bull. Pharm., Detroit, 1905, v. 19, p. 314.

Remington, J. P., in a communication to the editor points out the reason why trade names were not used in the new pharmacopœia.—*Ibid.*, p. 344.

The editor in discussing "Trade names in the new pharmacopœia" considers the general question of property right in an invention.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 301.

"Gnomon" comments on the article in the Druggists Circular and calls attention to the growing custom of registering trade-marks before taking out letters patent, so as to secure the continuance of trade-mark rights after the expiration of the letters patent.—*Pharm. J. Lond.*, 1905, v. 21, p. 442.

The editor discusses the abuses that have arisen in Germany in connection with the protection that is granted for the name of a medicinal article.—*Apoth. Ztg. Berlin*, 1905, v. 20, p. 902.

Rathenau, an attaché of the imperial (German) patent office, has published a lengthy dissertation on the rights and the limitations of trade names. The article is abstracted at some length.—*Ibid.*, p. 665.

An unsigned article comments at some length on an article on the United States and French trade-mark laws as contrasted with those of Germany and the South American Republics.—*Nat. Drug.*, St. Louis, 1905, v. 35, p. 264.

4. NEW REMEDIES.

Bearing closely on the admission of synthetic products into the pharmacopœia is the question of regulation of new remedies that is being discussed in various parts of the world.

The inauguration of the council on pharmacy and chemistry of the American Medical Association attracted considerable attention, and the work done by this council and by other bodies in different parts of the world will no doubt do much to differentiate between the true and the false in new remedies.

The rules of the council on pharmacy and chemistry are designed as requirements with which new remedies are expected to comply.—*J. Am. M. Ass.*, Chicago, 1905, v. 44, p. 718-721.

A circular letter signed by the presiding officers of the German, Austrian, and Swiss pharmaceutical societies calls attention to the need for definite and authentic information regarding new remedies and outlines suggestions as to the form in which this information is to be given.—*J. d. Pharm. v. Elsass-Lothr. Mülhausen*, 1905, v. 32, pp. 136-140.

Golaz-Vevey is credited with criticising the nomenclature of new remedies, which depends altogether too greatly on an ending in al, en, ic, in, or ol, of a name that is frequently fantastic, or at best based but loosely on the chemical composition or the therapeutic possibilities of the new remedy. He outlines the following as being indicative of the information that the apothecary should have:

- (a) The commercial as well as the exact chemical name.
- (b) Satisfactory tests for identity and purity.
- (c) Melting and boiling points.

- (d) Solubility factors.
- (e) Dose and uses.
- (f) Special incompatibilities.
- (g) Necessary precautions for keeping.

Ibid., pp. 143-145, etc.

Barthe, L., and others propose the establishing of official laboratories for the examination of new remedies and determining their composition.

Vidal, L., discusses this proposition at some length and considers such a central bureau as being a necessity. He also quotes the literature and gives a number of references bearing on this subject.—*Bull. Sc. pharmacol.*, Paris, 1905, v. 12, pp. 223-226.

Barthe, L., discusses the subject further, and his article is followed by one from G. Pégurier.—*Ibid.*, pp. 336-337 and 338-339.

Zernik, F., recounts the new remedies and innovations recorded during the year just past.—*Ber. d. pharm. Gesellsch.*, Berl., v. 15, 1905, p. 6 ff.

Riedel, in a review covering 52 pages, gives a summary of the new remedies introduced during the year 1904.—*Riedel's Mentor*, 1905, pp. 79-131.

Astre, Ch., gives a review of the composition and therapeutic properties of a number of the newer synthetics and makes an attempt to classify them and to determine their action and uses from their chemical composition.—*Bull. de Pharm. du Sud-Est*, 1905, v. 10, pp. 169-178.

Schieffelin, Wm. Jay, in an abstract of a paper presented at the Lewis and Clark Pharmaceutical Congress outlines the history of synthetic remedies and their manufacture.—*Am. Druggist*, N. Y., 1905, v. 47, p. 67, ff.

5. DOSES.

Leffman, Henry, feels that one effect of giving the dose of the various remedies will be to encourage the putting up of medicines by druggists without a physician's prescription. He also expresses the fear that the prescribing of "average doses" may lead to overdosing.—*Med. News*, N. Y., 1905, v. 87, p. 1276.

Wilbert, M. I., quotes the directions of the convention with reference to doses, and says:

In executing these indisputably plain and explicit instructions the members of the committee on revision can not be said to have followed them too closely.—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 357.

Williams, S. W., criticises the metric dose and its equivalent in the old system as presented in the pharmacopœia.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 308.

"Gnomon" comments on "suggested metric equivalents" for some doses commonly used in the British Pharmacopœia.—Pharm. J., London, 1905, v. 21, p. 420.

Van Schoor, Oscar, gives a comparative table of maximum doses in the new Italian (1903) and in the Belgian Pharmacopœia of 1885, also some comment on the variability of the doses in the Italian Pharmacopœia.—J. de pharm. d'Anvers, 1905, v. 61, pp. 53-55.

The Spanish Pharmacopœia is quoted as defining the term "dose" as "the quantity of medicine administered each time, or in each dose, to an adult male."—Brit. & Col. Druggist, Lond., 1905, v. 48, p. 420.

6. NOMENCLATURE.

The section on pharmacology and therapeutics recommended for adoption by the house of delegates of a resolution endorsing the nomenclature and orthography of the U. S. Pharmacopœia and urging that the American Medical Association adopt the U. S. Pharmacopœia as the standard of nomenclature and orthography in all its transactions and publications.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 71.

Herting, Otto, in discussing the variations that are to be found in the Latin titles for the same article in different pharmacopœias, expresses the fear that it might be considered too idealistic to have the Latin titles in all the pharmacopœias of the civilized world to correspond.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 127.

Lyons, A. B., thinks that in general the nomenclature evidences a conservative attitude wisely maintained. He discusses a number of individual titles and expresses regret at finding such barbarisms as "alcoholis" and "amyliis."—Proc. Am. Pharm. Ass., 1905, v. 53, p. 260.

Kleinschmidt, A. A., in discussing a few of the defects of our new Pharmacopœia bewails the inconsistency in the use of English synonyms.—*Ibid.*, p. 404.

Nixon, C. F., asserts that in no case can it be said that the change in nomenclature is in the interest of "accuracy or safety in dispensing."—Apothecary, Boston, 1905, v. 17, p. 774.

Williams, S. W., commends the changes that have been made in nomenclature.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 308.

The editor comments on the "fantastic" Latin of the U. S. Pharmacopœia, particularly the word "fluidextractum."—Répert. de Pharm., Paris, 1905, v. 17, p. 479.

Under the caption "Horrendous onomatology" the editor discusses some of the new titles found in the pharmacopœia.—Am. Druggist, N. Y., 1905, v. 47, p. 1.

Changes in nomenclature further discussed.—*Ibid.*, p. 63.

"Xrayser" points out that some of the Latin titles can hardly be "Augustan;" also expresses regret at the continuance of a number of doubtful titles and the introduction of such pedantic barbarisms as sulphonmethanum and sulphonethylmethanum.—Chem. & Drug., Lond., 1905, v. 67, p. 89.

He also discusses "the historic details furnished by the secretary of the pharmacopœial convention."—*Ibid.*, p. 439.

Wilbert, M. I., discusses changes in nomenclature.—Am. J. Pharm., Phila., 1905, v. 77, p. 359.

Greuel, Gustav, discusses the origin of a number of the older drug and plant names and outlines or suggests how many of these old names have been continued in modern botanical literature.—Pharm. Ztg., Berlin, 1905, v. 50, p. 621.

Hantzsch, A., points out the need for differentiating between true acids and pseudo-acids. Outlines some suggestions in this connection.—Ber. d. deutsch. chem. Gesellsch., 1905, v. 38, pp. 998-1004.

Schimpf, Henry W., discusses the nomenclature of chemical substances and expresses regret that the spelling adopted by the A. A. A. S. has not been followed.—Am. J. Pharm., Phila., 1905, v. 77, p. 553.

The editor commends the refusal to adopt the new chemical nomenclature in which the final *e* is dropped from the names of alkaloids and haloids.—Am. Druggist, N. Y., 1905, v. 47, p. 2.

Hinrichs, Carl G., discusses the changes that have been made in the "unchangeable" Latin titles.—Am. J. Pharm., Phila., 1905, v. 77, p. 506.

7. CHEMICAL FORMULAS.

Sayre, L. E., believes that the addition of the structural formula in the U. S. P. is pleasing and instructive to one who is interested in chemistry.—Pharm. Era, N. Y., 1905, v. 34, p. 412.

Hinrichs, Carl G., points out that while these formulas are of interest to theoretical and working chemists the molecular formula tells all that is required by the analytical chemist.—Am. J. Pharm., Phila., 1905, v. 77, p. 506.

Caspari, Charles E., commends the introduction of structural formulas as tending to show how a compound is derived and how it will break down under certain conditions.—Meyer Bros., Druggist, St. Louis, 1905, v. 26, p. 249.

Lyons, A. B., says "the completely 'analysed' form seems pure pedantry, but the plan if adopted should be carried out consistently." He points out a number of exceptions.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 261.

8. ASSAY PROCESSES.

Sayre, L. E., points out that the requirement of assay for so many drugs will materially change the responsibility of the pharmacist

and will discourage the so-called "hand-me-down" druggist.—Pharm. Era, N. Y., 1905, v. 34, p. 125.

Coblentz, Virgil, discusses the criticism that the apothecary will be unable to assay his drugs and preparations because the methods are too scientific or too complicated.—Apothecary, Boston, 1905, v. 17, p. 856.

Caspari, Charles E., points out the need of including the assay processes of the pharmacopœia in the curriculum of every college of pharmacy and asserts that no man has a moral right to dispense preparations whose strength he is unable to determine.—Meyer Bros., Druggist, 1905, v. 26, p. 248.

The editor in commenting on the practicability of the official assay processes says "it will be exceedingly interesting to watch the effect of the introduction of so many assayed drugs into the pharmacopœia."—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 263.

Wilbert, M. I., discusses the general principle involved and points out that it will require a considerable number of experiments by different operators to determine whether or not the adopted processes "lead to fairly uniform results in different hands."—Am. J. Pharm., Phila., 1905, v. 77, p. 360.

Mayer, Joseph L., makes a plea for the extension of assay processes to all drugs and preparations that are liable to form the basis of prosecution under drug adulteration enactments.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 477 (from Drug. Circ.).

Lyons, A. B., discusses the general subject of alkaloidal assay and suggests that some of the official processes may be criticised on the ground that they seem to be too much simplified.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 259.

Caeser and Loretz, in the introduction to their annual report, call renewed attention to the need for restricting tests and methods of assay to such as may be carried out in the laboratory of the well-equipped apothecary, with the simplest means, in the shortest time, and in the simplest way.—Geschäfts-Bericht v. Caeser & Loretz, i. Halle, a. S. 1905.

Vandkerleed, Charles E., outlines a method for assay of the emodin-yielding drugs.—Proc. Penna. Pharm. Ass., 1905, p. 193.

Gordin, H. M., describes a combination percolator and shaking tube for the assay of alkaloidal drugs, and a simple arrangement for percolation with hot alcohol.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 386–387.

Thoms, H., discusses the determination of alkaloids by means of potassium bismuth iodide.—Ber. d. pharm. Gesellsch., Berlin, v. 15, 1905, p. 85, ff.

An unsigned article enumerates and discusses the assay methods that have been published during the past year.—*Pharm. Weekbl.*, 1905, v. 42, pp. 67-70 & 174-177.

Puckner, W. A., reviews the literature relating to the estimation of alkaloids.—*Pharm. Review*, Milwaukee, 1905, v. 23, pp. 175 and 206, ff.

Fromme, G., discusses ammonia as a disturbing factor in the titrimetric estimation of alkaloids and points out that ether will dissolve considerable quantities of ammonia and of ammonia derivatives and that the ethereal extract of an alkaline extractive is not suited for direct titrimetric estimation of alkaloids.—*Geschäfts-Bericht v. Caeser & Loretz*, i. Halle, a. S., 1905, p. 14, ff.

The same author also discusses the use of aliquot parts, in place of the total extractive of the drug, in reply to objections that have been made by Puckner, Panchaud, and others.—*Ibid.*, p. 28, ff.

Dott, D. B., offers some criticisms of the official monographs on certain opium alkaloids, particularly the solubility.—*Abstr. Year Book Pharm.*, Lond., 1905, p. 120 (from *Pharm. J. Lond.*).

9. PURITY AND STRENGTH OF PHARMACOPŒIAL ARTICLES.

The editor commends the "purity rubric" as being opportune.—*Canad. Pharm. J.*, Toronto, 1905, v. 39, p. 20.

Lyons, A. B., discusses the "purity rubric," points out the possibility of differences in results obtained by various methods of analysis, and asserts that "no statement of a purity requirement should be made without a specification of the method to be used in making the necessary determinations."—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 258.

Hinrichs, Carl G., characterizes the "purity rubric" as a "very peculiar feature" of the new pharmacopœia in that it demands a strength which chemicals shall attain without prescribing a definite method of verification.—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 511.

Wilbert, M. I., discusses the general subject of purity and strength and questions the propriety of "more accurately defining the limit of *purity permissible* in official chemical substances."—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 361.

In a discussion of the general subject of quality *vs.* price, at the meeting of the Illinois Pharmaceutical Association a number of points of a practical nature are recorded.—*Proc. Ill. Pharm. Ass.*, 1905, pp. 96-112.

Nixon, C. F., believes that in common with some of the former revisions the standards of the pharmacopœia are so high that they are unattainable.—*Apothecary*, Boston, October, 1905, v. 17, p. 774.

Coblentz, Virgil, asserts that for inorganic chemicals the standards set represent the average samples as now marketed by reputable chemical manufacturers.—Apothecary, Boston, 1905, v. 17, p. 856.

10. STANDARDIZATION.

Patterson, A. G. C., in an address to the Chemists Assistants Association, asserts that it would be "a great calamity should the Ph. Brit. follow the lead of the U. S. P.," and include standards for drugs except in such cases where medical men and the public safety demand it.—Pharm. J., Lond., 1905, v. 21, p. 529.

Humphrey, John, deplores the tendency of the pharmacists to make assumptions with regard to active principles before the medical man has decided upon his requirements.—Am. Druggist, N. Y., 1905, v. 47, p. 232.

Maben, Thomas, discusses the extensive application of the principles of standardization and gives some historical references.—Pharm. J., Lond., 1905, v. 21, p. 139; see also Year Book of Pharmacy.

The subject is also discussed at some length by Naylor in the course of his address as president of the British Pharmaceutical Conference.—*Ibid.*

Dixon, W. E., discusses the bio-chemical standardization of drugs and points out that this method should be resorted to only when the chemical method is inadequate.—*Ibid.*, p. 155.

"Gnomon" questions the value of physiological standardization.—*Ibid.*, p. 690.

11. CHANGES IN STRENGTH.

Wilbert, M. I., discusses the changes in strength of the official preparations, and incidentally calls attention to the omission of caution notices in connection with tincture of cantharides and tincture of capsicum.—Am. J. Pharm., Phila., 1905, v. 77, p. 363.

Nixon, C. F., suggests that it should be the aim of revision committees to make as few changes as possible rather than as many as possible.—Apothecary, Boston, 1905, v. 17, p. 774.

See also comments under "Brussels Conference."

12. GENERAL FORMULAS.

The editor comments on the fact that "general formulas" have not been included for such preparations as lozenges, fluid extracts, or tinctures.—Pharm. J., Lond., 1905, v. 21, pp. 26-27.

Wilbert, M. I., discusses the general subject and compares the resulting number of preparations with the comparative number of preparations found in the German Pharmacopœia. Also deprecates the absence of general directions for making or dispensing some of the widely used preparations not provided for in the pharmacopœia.—Am. J. Pharm., Phila., 1905, v. 77, p. 354.

Sennewald, E. A., suggests that in the formulas themselves the ingredients be enumerated in the order in which they are to be mixed or manipulated.—Meyer Bros., Druggist, St. Louis, 1905, v. 26, p. 375.

13. WEIGHTS AND MEASURES.

Francis, John M., points out that opposition to the metric system still exists and that its use is felt by many to entail a great deal of vexation. The general use of this system may be delayed until the present generation of physicians and druggists shall have passed away.—Bull. Pharm., Detroit, 1905, v. 19, p. 275.

The editor suggests that a most serious shortcoming in the present pharmacopœia is the failure to give equivalents in ordinary measures.—The New Idea, 1905, v. 27, p. 137.

The editor, in discussing "How to dispense with equivalents," suggests that equivalents, which are dangerous things to fool with at best, may be flung to the winds if a couple of dollars be invested in a set of metric weights and measures.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 420.

The Lancet in discussing weighing *versus* measuring, as applied to the dispensing of medicines, asserts that dispensers should continue to be guided by the rule: "Solids by weight and liquids by measure."—Abstr. in Pharm. J., Lond., 1905, v. 21, p. 342.

"Gnomon" in discussing the coming of the "mil" points out that this name has many and varied advantages over the more cumbersome term "cubic centimeter," and recommends that the word "mil" be widely used to designate the one-thousandth part of a liter.—*Ibid.*, p. 32.

Wilbert, M. I., asserts that the approximate measures of the U. S. P., VIII, are neither decimal in character nor approximately correct; the accuracy of this assertion was demonstrated by the exhibition of a series of plaster casts of various kinds of spoons.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 301-304.

14. ADDITIONS AND DELETIONS.

Wilbert, M. I., points out that previous revision committees were more than usually careful in the consideration of dismissals and that of the many articles dismissed by the revision committees of 1880 and 1890 but three were considered worth reconsideration by the present committee.—Am. J. Pharm., Phila., 1905, v. 77, p. 364.

Remington, J. P., expresses the wish that "we could have had in the pharmacopœia more preparations."—Proc. Am. Pharm. Ass., 1905, v. 53, p. 255.

Thornton, E. Q., says it is a pity that a number of the inert or antiquated drugs of the pharmacopœia were not discarded.—Therap. Gaz., Detroit, 1905, v. 29, pp. 732-740.

The editor discusses a number of preparations which he considers as being questionable expurgations.—*Ibid.*, p. 597.

Marshall, C. R., points out that because a drug is prescribed by a few, or even by many, medical men is not sufficient reason for it to be introduced into a pharmacopœia.—*Pharm. J., Lond.*, 1905, v. 21, p. 716.

15. DROPS AND DROPPERS.

Williams, S. W., expresses regret that the Pharmacopœial Revision Committee did not include the provisions for defining a normal drop counter, as recognized by the French Codex more than twenty years ago.—*Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 308.

Wilbert, M. I., calls attention to the action of the International Conference for the Unification of Potent Medicaments and deprecates the general lack of interest that was manifested by the committee of revision in the proceedings of this congress.—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 367.

"Gnomon" recommends the pipette used in France, which delivers "what may be regarded as standard drops" twenty to the gramme or mil of distilled water.—*Pharm. J., Lond.*, 1905, v. 21, p. 362.

Yvon, M. P., discusses a normal drop-counting device and its application in practical pharmacy. The paper includes a careful study of the several factors which tend to influence the size and weight of drops.—*Répert. de Pharm., Paris*, 1905, v. 17, pp. 391-395.

Koren, Aug., jr., describes a new dropping device, by means of which he can regulate the size of drops within quite a wide range.—*Abstr. in Pharm. Ztg. Berlin*, 1905, v. 50, p. 582, from *Tidskr. f. Kem. u. Farm.*

See also Normal drop counter under "Brussels Conference."

16. POWDERED DRUGS.

Wilbert, M. I., discusses the motion (see p. 22) adopted on the second day of the convention and points out that in respect to powdered drugs the U. S. P., VIII, is decidedly behind the German Pharmacopœia.—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 367.

The Spanish Pharmacopœia contains detailed directions for powdering some fifty of the more important drugs, or practically all that are used in the powdered form.—*Farmacopea Oficial Española*, 1905, pp. 479-490.

Nelson, Burt E., makes some attempt at classifying powdered drugs according to the structure and the content of the several cells. (List of drugs, so far described, included in, *Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 611.)—*Merck's Rep.*, N. Y., 1905, v. 14, p. 37, et seq.

The editor makes a facetious reference to the provisions for fineness of powders as given in the U. S. P., VIII.—*Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 267.

3. ANALYTICAL DATA.

1. ADULTERATIONS.

Lloyd, John Uri, discusses the several definitions for adulterations and substitutes that have been presented, and interprets them as follows:

An adulteration is a substance mixed, or designed to be mixed, with a drug (or other substance) for the purpose of cheapening the drug, thus, brick dust becomes an adulterant when mixed with powdered bloodroot. A substitute (commercial) is a substance offered or sold in place of another, thus, willow twigs sold under the name "willow herb" is a commercial substitute but not a therapeutic substitute. A therapeutic substitute is a substance nearly or quite paralleling another, or similar to another, in its therapeutic action, thus, the physician who desires a tonic, say, gentian, which, however, is out of his reach, may substitute for it quassia, another tonic.—Pharm. Review, Milwaukee, 1905, v. 23, p. 284, ff.

Schleimer, A., points out that if dealers would see that they get exactly what they pay for there would be no need of pure drug laws; the amount of adulteration would in a short time be reduced to a minimum, and it would not be long before it would be practically unknown. In the matter of drugs, for instance, he points out that though the retail druggist does not adulterate he is the one who should be held responsible, because he is expected to examine, test for, and detect adulterants in the goods that he buys.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 342.

The editor in commenting on the above article points out the all too frequent mistaken use of the words "adulteration" and "substitution."—*Ibid.*, p. 340.

Rusby, H. H., defines adulteration in the strict sense as an intentional fraudulent act, and, in the broad sense, as anything which results in the purchaser's receiving something different from that which he desires and supposes himself to be receiving.—Drug Topics, N. Y., 1905, v. 20, pp. 152-154.

Rusby, H. H., in discussing the prevention of adulteration, points out the need for insisting that no drugs be sold under any other than their legitimate and proper names, and suggests that wholesale dealers employ capable and qualified persons who would be able to detect errors and see that adulteration is reduced to a minimum. Merck's Rep., N. Y., 1905, v. 14, p. 212.

Kebler, L. F., in an address made at the meeting of the International Food Congress, discusses adulteration, fakes, and frauds.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 224.

Kebler, L. F., in a paper presented at the meeting of the A. Ph. A., discusses the adulteration of chemicals and cites a number of substances that were found to be contaminated or in other ways below

the standards set for them.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 268–271.

In an abstract or news note attention is called to an announcement sent out by a firm in Marseille who offer to supply ground and powdered almond shells, which they point out are useful as an admixture to chocolate, biscuits, drugs, and spices.—Pharm. Ztg., Berlin, 1905, v. 50, p. 561.

The committee on adulteration, of the N. W. D. A., points out that—

If adulterated articles find their way into commerce to-day it is accomplished knowingly and wilfully, because published tests pertaining to most every article of commerce may be readily obtained from manufacturers who publish them with the sole object of educating the buyer to existing standards.—Paint, Oil, and Drug Rep., 1905, p. 15, Oct. 6.

2. ANALYTICAL METHODS AND RESULTS.

Hinrichs, Carl G., criticises the gasometric analysis of the new pharmacopœia and asserts that “the gas burette (nitrometer) used is not the best, cheapest, or most practical style for the druggist or chemist”.—Am. J. Pharm., Phila., 1905, v. 77, p. 507.

Kreider, L. L., describes and discusses the use of apparatus for the determination of volatile substances, particularly carbonates and ammonium salts.—Ztschr. f. anorg. Chem., 1905, v. 44, pp. 154–157.

Folin, Otto, discusses sulphur and sulphate determinations.—J. Biol. Chem., 1905, v. 1, pp. 131–159.

Utz discusses the use of the various forms of refractometer and the application of this instrument in the pharmaceutical test laboratory.—Pharm. Prax., 1905, v. 4, pp. 502–504.

Reichard, C., discusses the recommendations that have been made by M. E. Schuyten for the use of antipyrine as a reagent for nitrites, the complications that may arise, and suggests that this reaction is reliable only as a qualitative not as a quantitative test.—Pharm. Prax., 1905, v. 4, p. 12.

Boetticher, H., outlines a scheme for the separation of the metals of the ammonium sulphide group.—Abstr. *Ibid.*, p. 11.

Brunker, J. E., reports upon the results obtained from the analysis of pharmaceutical preparations by the analysts of the Poor Laws Unions of Ireland.—Pharm. J. Lond., 1905, v. 21, p. 134.

3. REAGENTS.

Kebler, L. F., describes the precautions that have been adopted in connection with the drug laboratory of the Bureau of Chemistry to insure the acceptance of reliable chemicals only.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 80.

Kebler, L. F., as chairman of the committee on testing of chemical reagents, describes the outline suggestions that were sent out to chemists for the examination of a number of widely used reagents.—*Proc. Ass. Off. Agr. Chem.*, 22 Ann. Conv. [1905], 1906, pp. 183-184.

Gardner and North, as the result of a series of experiments with solutions of potassium permanganate and of ammonium oxalate, conclude that the latter readily deteriorate and are no longer reliable after, at most, eight days.—*Abstr. in Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 17.

Biltz, H., describes and figures a modification of the sulphuretted hydrogen apparatus designed by Cl. Winkler.—*Abstr. in Pharm. Ztg.*, Berlin, Aug. 19, 1905, v. 50, p. 695.

Rupp, E., discusses the use of iodic acid as a reagent, and reports a series of experiments to demonstrate its efficiency as a reducing agent.—*Arch. d. Pharm.*, 1905, v. 243, p. 98, ff.

Alvarez, E. P., discusses a new color reagent for the polyphenols, their isomers and higher organic compounds. He also records observations on diphenylamine as a reagent for nitrites, nitrates, and chlorates, and its use when mixed with resorcin and beta-naphthol.—*Chem. News, Lond.*, 1905, v. 91, pp. 125, ff, 155.

Sorensen and Andersen discuss the use of sodium carbonate in acidimetry, and outline the precautions that must be observed to avoid errors.—*Ztschr. f. analyt. Chem.*, 1905, v. 44, pp. 156-184.

Worden and Motion discuss the preparation of volumetric solutions and conclude that the most accurate and the most easily performed method is that of taking the specific gravity in carefully calibrated picnometers. A number of tables are included.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 178-182.

4. ATOMIC WEIGHTS.

Francis, John M., says that the conservative course of retaining "H=1" as the unit, while waiting to settle the controversy over H=1 or O=16, has the advantage of retaining the system hitherto in vogue.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 275.

Leffman, Henry, views with disfavor the adoption of the atomic weights based on H=1 instead of O=16.—*J. Am. M. Ass.*, Chicago, 1905, v. 45, p. 1440.

Hinrichs, Carl G., criticises the statement made in the preface of the pharmacopœia regarding the atomic weight table used, deprecates the decision that has been made, and asserts that "the U. S. P. will stand for years to come as a relic of the past."—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 512.

Wilbert, M. I., discusses the atomic weight table and compares the molecular weights of a number of compounds based on the atomic

weights of the U. S. P., VIII, of the U. S. P. (1880), of the Ph. Germ., IV, and of the U. S. P. (1890).—*Ibid.*, p. 368.

The Spanish Pharmacopœia contains a table of atomic weights based on $O=16$ and $H=1.008$.—*Farmacopea Oficial Española*, 1905, p. 19.

The Netherlands Pharmacopœia also includes an atomic weight table based on $O=16$ and $H=1.008$.—*Pharmacopea Nederlandica*, 1905, p. 524.

The report of the international committee on atomic weights announces that the vote of the larger committee has decided in favor of publishing a single table of atomic weights in future, based on $O=16$, in place of the double table formerly published.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 7.

Meyer, Julius, discusses the methods followed in the estimation of atomic weights and outlines some suggestions on the estimation of atomic weight mathematically.—*Ztschr. f. anorgan. Chem.*, 1905, v. 43, pp. 242–250.

Werner, A. discusses the periodic system, with a proposed elaboration and systematic arrangement of the elements.—*Ber. d. deutsch. chem. Gesellsch.*, 1905, v. 39, pp. 914–921.

Hanssen, C. J. T., reports on the weights of oxygen, nitrogen, and hydrogen.—*Chem. News, Lond.*, 1905, v. 92, p. 2394.

Leduc, A., discusses the atomic weights of hydrogen and nitrogen.—*Compt.-rend. Acad. d. sc. Paris*, 1905, v. 140; abstract in *Chem. News, Lond.*, v. 91, p. 176.

Guye, Phillippe A., reports new researches on the atomic weight of nitrogen.—*Chem. News, Lond.*, 1905, v. 92, pp. 261, 275, 285.

Gray, Robert Whytlaw, discusses the atomic weight of nitrogen.—*J. Chem. Soc. Lond.*, 1905, v. 87, part 2, pp. 1601–1620.

Dixon, Harold B., and Edgar, E. C., discuss an attempt to determine the equivalent of chlorine by direct burning with hydrogen.—*Chem. News, Lond.*, 1905, v. 91, p. 37.

Baxter, George Paul, discusses the revision of the atomic weight of iodine.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 876–887.

Köthner and Aeuer discuss the atomic weight of iodine.—*Chem. News, Lond.*, 1905, v. 91, p. 37.

Richards and Wells discuss the atomic weights of sodium and chlorine.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 459–528.

Parsons, Charles Lathrop, contributes a note on the atomic weights of carbon and beryllium.—*Ibid.*, pp. 1204–1206.

5. INDICATORS.

Clowes, G. H., discusses the theory of indicators and its bearing on the analysis of physiological solution by means of volumetric methods.—*Abstr. in J. Am. Chem. Soc.*, 1905, v. 27, p. 452.

Schwezew, B., reviews the work that has been done with the color from red cabbage and gives some account of its uses as an indicator.—*Pharm. Ztg. Berl.*, 1905, v. 50, p. 990.

Puckner, W. A., calls attention to the fact that N. Gray Bartlett proposed the use of the coloring matter of red cabbage as an indicator more than twenty years ago.—*Pharm. Review*, 1905, v. 23, p. 375.

Scholtz, M., discusses the use of mixed indicators in connection with titrimetric estimations of acids and alkalies.—*Abstr. in Pharm. Prax.*, 1905, v. 4, p. 12 (from *Ber. d. pharm. Gesellsch.*).

CUDBEAR.

Tollman, L. M., outlines a method for differentiating between coal-tar colors and lichen colors.—*Abstr. in Analyst*, London, 1905, v. 30, p. 213.

Parisen, Geo. W., gives a formula and outlines a method for preparing tincture of persionis.—*Proc. N. J. Pharm. Ass.*, 1905, p. 74.

CURCUMA.

Leach, A. E., discusses the composition of turmeric.—*Brit. Food. J.*, 1905, v. 6, p. 252; reference from *Index Medicus*, 1905, p. 299.

Arzberger discusses the demonstration in powdered rhubarb of curcuma, by the use of chloroform and ether as solvents.—*Abstr. in Deut.-Amer. Apothek. Ztg.*, N. Y., 1905, v. 26, p. 33 (from *Ztschr. d. allgem. österr. A. V.*).

Linde, O., discusses the detection of curcuma and points out that other vegetable drugs give similar color reactions with sulphuric acid.—*Abstr. in Ztschr. f. Unters. d. Nahr. u. Genussm.*, Berlin, 1905, v. 9, p. 696 (from *Pharm. J.*).

6. ASH DETERMINATIONS.

Caeser and Loretz outline a method of making ash determinations, which they recommend for routine use. A porcelain crucible is filled to about one-third of its capacity with sand and the whole heated to redness, then placed in an exsiccator until cool, and weighed. A quantity of drug is then placed on the sand and the total weight determined. The material is then placed in a drying closet for an hour and heated to about 100° C., the weight again taken, to determine the loss on drying, and the crucible then heated to redness to carbonize the contained material. After allowing the crucible to cool slightly, the carbonized material is thoroughly mixed with the sand and the mixture again heated to redness until all of the carbon has been burned off. Should combustion be delayed, it may be advisable to allow the mixture to cool slightly, shake the sand to one side and add from five to ten drops of fuming nitric acid, then heat again, and finally add a small quantity of oxalic acid to decompose

the formed nitrates. After allowing the crucible to cool, place it in an exsiccator for half an hour and weigh.—Geschäfts Bericht v. Caesar & Loretz, i. Halle a. S., 1905, p. 83, ff.

Gutzeit, E., recommends a method for the determination of ash in vegetable drugs. This involves the use of freshly calcined basic calcium phosphate, which is also described.—Abstr. in Proc. Am. Pharm. Ass., 1905, v. 53, pp. 700 and 714 (from Pharm. Ztg.).

Wüthrich, E., recommends the addition of oxalic acid to aid combustion in ash determinations.—Abstr. in Pharm. Zentralh., 1905, v. 46, p. 555 (from de Suikerindustrie).

7. SPECIFIC GRAVITY.

The editor, while commending the adoption of 25° C. for specific gravities and solubilities, adds:

It is nevertheless to be regretted that the equivalent specific gravities and solubilities were not stated at 15° C. also, not only for comparison with a standard which is now being used abroad, but in order to obviate the necessity, on the pharmacist's part, of purchasing instruments adapted for use at 25° C. or else making tedious compensatory calculations or comparisons with instruments graduated at 25° C.—Merck's Rep., N. Y., 1905, v. 14, p. 284.

Want, W. Philip, points out that the adoption of 25° C. as the temperature for determining specific gravity, though no doubt *per se* a convenience in America, has this drawback that the results obtained will not be directly comparable with European figures.—Am. Druggist, N. Y., 1905, v. 47, p. 96.

Hinrichs, Carl G., asserts that "the normality introduced will prove practical for the determination of the strength of weak solutions of acids and alkalies, not, however, for the higher strengths above 10 per cent.—Am. J. Pharm., Phila., 1905, v. 77, p. 512.

v. Wrochem, J., describes and outlines the method of using an apparatus designed to facilitate the determination of the specific gravity of substances in powder form.—Chem. Ztg. Cöthen, 1905, v. 29, p. 1034.

Ferguson, W. C., describes the methods employed in preparing the tables of specific gravity of sulphuric acid, nitric acid, hydrochloric acid, and ammonia that were adopted by the Manufacturing Chemists' Association of the United States.—J. Soc. Chem. Ind., Lond., 1905, v. 24, pp. 781-790.

8. SOLUBILITIES.

Hinrichs, Carl G., says:

Solubilities are given now at 25° C. This makes a difference, as a rule, from the 1890 data of about 5 per cent. on the amount dissolved.—Am. J. Pharm., Phila., 1905, v. 77, p. 511.

Kahlenberg, Louis, discusses the theories that have been advanced concerning the phenomena of solution.—Chem. Ztg. Cöthen, 1905, v. 29, p. 1081.

Martin. Geoffrey, offers a contribution to the theory of solution in which he seeks to explain the nature of solution by considering the forces brought into play when a foreign molecule is introduced among the molecules of a solvent.—Abstr. in *J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 388 (from *J. Phys. Chem.*).

Herz and Knoch, in a contribution on solubilities in mixtures of solvents, enumerate a number of substances and discuss their solubility in mixtures of acetone and water, mixtures of alcohol and water, and in mixtures of alcohol and glycerin.—*Ztschr. f. anorgan. Chem.*, 1905, v. 45, pp. 262-269.

Hulett, G. A., discusses solubility and size of particles. He concludes that the influence of size of particles seems to be of the same order of magnitude for different substances, and is therefore especially a source of error when very slightly soluble substances are used.—Abstr. in *J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 447.

Philip, James Charles, discusses the influence of various sodium salts on the solubility of sparingly soluble acids.—*J. Chem. Soc. Lond.*, 1905, v. 87, pp. 987-997.

Foote, H. W., discusses the solubility of potassium and barium nitrates and chlorides.—Abstr. in *J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 450.

Foote and Bristol discuss the solubility of barium and mercuric chlorides.—Abstr., *ibid.*, p. 450 (from *Am. Chem. J.*).

9. BOILING POINT DETERMINATIONS.

Riedel's *Berichte* includes a comprehensive review of a number of the boiling points that are given in the German Pharmacopœia with some discussion of the methods that are involved or recommended for their determination. Some attempt was also made to determine the boiling points of the several materials under varying conditions of atmospheric pressure. The point is made that the pharmacopœia should indicate whether or not a particular boiling point has been corrected and also state the barometric pressure for which it has been so corrected. It is further pointed out that the determination of the boiling point of a substance may be of value in connection with the determination of the purity of a substance, and it may be necessary to point out the direction in which variation from the official temperature may point to purity or impurity of a given substance.—Riedel's *Berichte*, Berlin, 1905, pp. 37-53.

10. MELTING POINT DETERMINATIONS.

Hinrichs, Carl G., discusses the fusing points enumerated in the new U. S. P. and points out that "the data of a pharmacopœia should be such as to admit of easy confirmation and be of practical value."—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 511.

Herting, Otto, regrets that the committee of revision did not include specific directions for determining the melting point of substances, as he considers this a factor of prime importance in determining the identity and the purity of chemical substances.—*Deut.-Amer. Apoth. Ztg.*, N. Y., v. 26, 1905, p. 72.

Guttman, Leo Frank, discusses the determination of melting points at low temperatures.—*Chem. News, Lond.*, 1905, v. 92, p. 8.

Hüttner and Tammann discuss the relation of the melting points of salts to the converting point from one crystalline form to another, coupled with some observations on the cooling curves.—*Ztschr. f. anorgan. Chem.*, 1905, v. 43, pp. 215–227.

Landsiedl, Anton, describes and figures an apparatus that is designed to facilitate the rapid and correct determination of the melting point of organic substances.—*Oesterr. Chem. Ztg.*, 1905, v. 8, p. 276.

Siedler, P., in a discussion of the melting points of the German Pharmacopœia, calls attention to the need for and the use of melting-point determinations, and describes the several methods that have been devised for making these determinations. Siedler prefers the apparatus devised by Gatterman.—*Pharm. Post, Wien*, 1905, v. 38, p. 568; also other pharmaceutical and chemical journals.

Ubbelohde, Leo, discusses the need for determining the temperature at which solid fats and wax-like substances tend to form drops. The author has designed and figures an apparatus which is intended to facilitate the determination of this factor.—*Ztschr. f. angew. Chem.*, 1905, v. 18, pp. 1220–1225.

11. THERMOMETRIC TABLES.

Hinrichs, Carl G., criticises the thermometric tables as being unreasonable and impractical. "There is no use going beyond that which can be detected with certainty. Chemists are happy if they get the tenth of a degree with certainty."—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 512.

12. POLARIZATION AND REFRACTION.

Walden, P., reviews the literature relating to the development of our knowledge of optically active bodies, the nature and number of optically active bodies, the mathematical designations that are used, the variability of the rotatory power, the influence of temperature on the rotary powers, the influence of wave lengths of light, solvents, the influence of time, and finally some attempts to explain the variability of the rotatory power.—*Ber. d. deutsch. chem. Gesellsch.*, 1905, v. 38, pp. 345–409.

Marckwald and Paul, in a preliminary publication, record some observations on the conversion of racemic bodies into the optically active varieties.—*Ibid.*, pp. 810–812.

Harvey, T. F., discusses some temperature corrections for use with the Abbe refractometer, and refractive indices of some fixed and essential oils.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 717-719.

13. FILTERS.

Shimer, Porter W., describes and figures a filter in which he uses, in place of the ordinary filter paper, a layer of felt over which he spreads a layer of pulped filter paper.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 287-292.

Gaedicke, R., describes and figures a perforated porcelain cone and an accompanying funnel which he believes will facilitate rapid and exact filtration in quantitative analysis.—*Abstr. in Pharm. Ztg., Berlin*, 1905, v. 50, p. 693 (from *Allg. Chem. Ztg.*).

14. OXIDATION.

Schaer, Ed., discusses the influence of alkaline substances on various oxidation processes.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 208-215.

Benrath, Alfred, refers to the oxidizing action of ferric chloride in sunlight.—*Abstr. (J. pr. Chem., 1905 (II), v. 72, pp. 220-227) J. Chem. Soc. Lond.*, 1905, v. 88, part 2, p. 730.

Schaer, Ed., reports a comprehensive study of autoxidation as manifested in color changes. The report includes data on (1) gallo-tannic acid, (2) pyrogallol, (3) chinon, (4) aloin (isobarbaloin, Leger), (5) chrysarobin, and (6) brasilin.—*Arch. d. Pharm.*, 1905, v. 243, p. 198, ff.

Ciamician and Silber report on a continuation of previous experiments on the reduction of nitrobenzene by the aid of light.—*Abstr. (Ber., 1905, v. 38, pp. 1176-1184 and 1671-1675) J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 461 and 641.

15. COLOR STANDARDS.

Schreiner, Oswald, describes and figures a simple colorimeter for general use and includes some additional remarks on colorimetric methods and apparatus.—*J. Am. Chem. Soc., N. Y.*, 1905, v. 27, pp. 1192-1203.

In an unsigned article a colorimeter designed by Otto Bismarck is described and illustrated.—*Oesterr. Chem. Ztg.*, 1905, v. 8, p. 277.

Lyons, A. B., describes some new color reactions.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 329-332.

Kraemer, H., discusses the origin and nature of color in plants.—*Proc. Am. Philos. Soc.*, 1905, v. 43, 257-277.

16. ALKALINITY OF GLASS.

Baroni (*Giorn. Farm. Chim.*, v. 53, p. 481) describes an easy method of testing the neutrality of glass, which depends on (1) the

coloration and precipitation of a solution of morphine hydrochloride; (2) the precipitation of strychnine nitrate; and (3) the precipitation and subsequent coloration of solutions of mercuric chloride.—*Abstr. J. Am. Chem. Soc.*, 1905, v. 27, p. 1351.

van Rijn (*Pharm. Weekbl.* v. 41, p. 1025) recommends cleaning the vessels with hydrochloric acid and water, then filling with distilled water containing phenolphthalein. There must be no reddening after fourteen days.—*Ibid.*, p. 1351.

Wetterstroem, Theo. D., points out that a portion of the loss of acidity and even an impairment of the esters in brandies and whiskeys is to be attributed to the alkalinity found in white glass of reputed purity.—*Drug. Circ. & Chem. Gaz.*, N. Y., v. 49, p. 312.

17. TESTS.

ACID, OXALIC.

Moissan (*Pharm. J.*, No. 3477, p. 845) shows that in the reaction between carbon dioxide and potassium hydride, at a temperature between 100° and 200° C., a quantity of oxalate is formed as well as formate.—*Abstr. Merck's Rep.*, N. Y., 1905, v. 14, p. 249.

Baxter and Zanetti (*Am. Chem. J.*, N. Y., v. 33, p. 500) outline a method for estimating oxalic acid in the presence of hydrochloric acid.—*Abstr. Pharm. Ztg.*, Berlin, 1905, v. 50, p. 603.

Patch, Edgar L., in report of committee on drug market, points out that oxalic acid frequently contains traces of nitric and sulphuric acids and of iron.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

ALKALINE MONOCARBONATES AND BICARBONATES.

Cowley and Catford discuss the determination of alkaline monocarbonates and bicarbonates and point out that the use of barium chloride is liable to yield erroneous results unless attention is paid to the proportion of barium chloride used.—*Pharm. J.*, Lond., 1905, v. 21, p. 864.

ALCOHOL, AMYL.

Lyons, A. B., suggests that not the least important requirement would be "it should leave no residue on evaporation."—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 262.

Beckmann, E. (*Ztschr. f. Unters. d. Nahrungsm.*, 1905, 1 & 2), outlines a method for the estimation of alcohol in alcoholic liquids, depending on the use of carbon tetrachloride as a solvent for the amyl alcohol.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 685.

Gadamer, J., reports observations on the action of amyl alcohol on chlorethylalcoholate, that were made to determine whether the latter could be made to exchange the ethyl group for the amyl group.—*Arch. d. Phar.*, 1905, v. 245, p. 30 ff.

Kebler, L. F., in report of committee on drug market, points out that samples of amyl alcohol were found to contain petroleum, from the use of petroleum barrels.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

Richmond and Goodson (*Analyst*, 1905, v. 30) point out that as much as 4 per cent of petroleum has been found in amyl alcohol, and suggest that amyl alcohol, which gives any visible insoluble layer when 2 cc. are treated with 10 cc. of water and 10 cc. of sulphuric acid, should not be used for testing milk.—*Abstr. J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 344.

Burford, S. F., also discusses impurities in amyl alcohol.—*Ibid.*, pp. 391-392.

ALCOHOL, METHYL.

Wiley, H. W., discusses the nature, the production, and the use of methyl alcohol.—*Am. J. Pharm.*, Phila., 1905, v. 77, pp. 101-106.

A discussion on the use of methyl alcohol.—*Ibid.*, p. 119-123.

Wetterstroem, Theo. D., asserts that wood alcohol is still much used as an adulterant, having been found in tincture of iodine, bay rum, witch hazel distillates, "patent" medicines, and hair tonics.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 313.

Patch, Edgar L., in the report of the committee on drug market, points out that 117 out of 2,121 samples of pharmaceutical, or 5.51 per cent, contained wood alcohol. (N. Y. Board of Pharmacy.)—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

Sadtler, S. P., discusses the tests that have been proposed and points out some of the advantages of the test that has been included in the new U. S. P., for the detection of methyl alcohol.—*Am. J. Pharm.*, Phila., 1905, v. 77 pp. 106-110.

Leach and Lithgoe review the methods that have been proposed for the detection of methyl alcohol in mixtures with ethyl alcohol and outline a method for recognizing the presence of methyl alcohol by means of the immersion refractometer.—*Tech. Quarterly*, 1905, v. 18, pp. 228-235.

The detection of methyl alcohol is also discussed by—

Scudder, Heyward.—*N. Y. Med. J.*, 1905, v. 81, pp. 1163-1164.

Kahn, Joseph.—*Am. Druggist*, 1905, v. 47, p. 3.

Peters, R.—*Pharm. Zentralh.*, 1905, v. 46, p. 521.

Fendler & Mannich.—*Pharm. Post*, Wien, 1905, v. 38, p. 568.

Gnehm & Kaufler.—*Abstr. J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 1339.

ARSENIC.

Caspari, Charles E., says the modified Gutzeit test for arsenic is in many cases entirely too rigid. In the first place, it is difficult to obtain reagents which by this test will not show the presence of arsenic, and, in the second place, many official chemicals should be permitted to contain more arsenic than is represented by the propor-

tion 1:100,000, which is the least permissible quantity of arsenic allowed by the pharmacopœia.—Meyer Bros., Druggist, 1905, v. 26, p. 248.

Hill, C. A. (Chem. and Drug., Lond., 1905, v. 67, p. 548), describes an effective method of applying the Gutzeit test for arsenic.—Ref. from Ind. Med., 1905, v. 3, p. 1137.

Lockemann, Georg, gives a comprehensive review of the literature relating to the use of the Marsh apparatus and its various modifications.—Zeitscher. f. angew. Chem., 1905, v. 18, pp. 416–429.

Pozzi (L'Industria Chimica, v. 6, p. 144) outlines a rapid method for the determination of arsenic by regulating the flow of hydrogen from a Marsh apparatus and slowly passing the arsine through a solution of tenth normal silver nitrate with ammonia. After three or four hours he acidifies the silver solution and determines the amount of undecomposed silver nitrate by means of potassium sulphocyanate, using ferric sulphate as an indicator.—Abstr. J. Am. Chem. Soc., 1905, v. 27, p. 1350.

Gautier, A. (Zeitschr. f. Unters. d. Nahr. u. Genussm.), recommends a method for the determination of small quantities of arsenic which depends on the fact that, in the oxidation and precipitation of iron, all of the arsenic that may be present in a solution is precipitated with the iron.—Abstr. Pharm. Prax., 1905, v. 4, p. 13.

Mai and Hurt (Zeitschr. f. Unters. d. Nahr. u. Genussm., 1905, v. 9, pp. 193–199) discuss an improved method of estimating arsenic electrolytically, and figure the apparatus.—Abstr. Exp. Sta. Rec., v. 17, No. 1, p. 7.

Frerichs and Rodenburg review the work that has been done on methods for the electrolytic determination of minute quantities of arsenic.—Arch. d. Pharm., 1905, v. 243, p. 328.

Hill and Collins describe and figure the apparatus used in an effective and simple method of applying the Gutzeit test.—Chem. & Drug. Lond., 1905, v. 67, pp. 548, 739.

Chapman and Law express a preference for cadmium chloride in place of stannous chloride.—*Ibid.*, p. 768.

Cantoni and Chautems (Arch. Sc. phys. nat. Genève, 19, p. 364–366) point out that arsenic can be separated from antimony by making use of the volatility of methyl arsenite at the ordinary temperatures.—Abstr. J. Soc. Chem. Ind. Lond., 1905, v. 24, p. 691.

Norton and Koch outline a method for the detection and the determination of arsenic and antimony in the presence of organic matter.—J. Am. Chem. Soc., N. Y., 1905, v. 27, pp. 1247–1251.

Miranda (Revista Farmacéutica Chilena) outlines differential reactions to distinguish methylarsenate, cacodylate, and arsenate of sodium.—Abstr. Répert. de Pharm. Paris, 1905, v. 17, p. 102.

Grimbert, L. (J. Pharm. Chim., v. 21, p. 385) reports on the presence of arsenic in hydrogen peroxide solution.—Year Book Pharm., Lond., 1905, p. 42.

Dunstan and Robinson (report presented to the Pharmacopœia Committee of the General Council) discuss the detection of arsenic in official drugs.—*Ibid.*, pp. 25–41.

Lobello, R., discusses the sensitiveness of the Bettendorf test for arsenic.—Boll. Chim. Farm., Milan, 1905, v. 44, pp. 445–446.

Ferraro and Carobbio outline a proposed modification of the Bettendorf test.—*Ibid.*, pp. 805–807.

Denigés, G., reports a critical study of the localization of arsenic in various parts of the body.—Bull. Soc. Pharm., Bordeaux, 1905, v. 45, pp. 129–141, 201, 203.

Blarez and Denigés report three cases of poisoning, with a detailed enumeration of the comparative amounts of arsenic found in the several portions of the bodies.—*Ibid.*, pp. 36–45.

Denigés, G. (Ann. de chim. et de phys., 1905), discusses the literature relating to the localization of arsenic and concludes that it is more particularly fixed by the liver substance.—Abstr. Biochem. Centralbl. 1905, v. 4, p. 546.

BARIUM, SALTS OF.

Skrabal and Neustadtl review the history of the use of chromates as reagents for barium, the preparation of the solutions, and the use of the resulting solution in varying mixtures for the precipitation of barium from strontium or calcium or from mixtures of the two.—Ztschr. f. analyt. Chem., 1905, v. 44, pp. 742–755.

Thorne, Normann C. (from the American Journal of Science, Silliman), discusses the precipitation of barium bromide by means of hydrobromic acid.—Ztschr. f. anorgan. Chem., 1905, v. 43, pp. 308–313.

Anoni, A. (Boll. Chim. Farm., 1905), outlines a method for preparing barium cacodylate which, in turn, he proposes as the basis of all other compounds of this class.—Abstr. Pharm. Ztg., Berlin, 1905, v. 50, p. 844.

Basch, E. E. (Chem. Ztg., 1905, v. 29, pp. 721–723), records some experiments in which barium carbonate used in excess and thoroughly mixed with the water was found to be an effective means of reducing hardness.—Abstr. Exp. Sta. Rec., v. 17, No. 4, p. 339.

Alcock, F. H. (Pharm. J., v. 19, p. 173), outlines a method for the volumetric determination of barium chloride by the use of sodium sulphate and titrating the resulting sodium chloride with silver nitrate, using potassium chromate as an indicator.—Year Book Pharm., Lond., 1905, p. 45.

Kebler, Lyman F., in committee on drug market report, points out that barium hydrate not infrequently contains fragments of hay, wood, and paper; also chloride and carbonate.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 183.

Hulett and Duschak (*Z. anorg. Chem.*, v. 40, pp. 196–217) have investigated and report on the presence of chlorine in barium sulphate precipitated by barium chloride.—*Abstr. J. Am. Chem. Soc.*, 1905, v. 27, p. 449.

BROMIDES.

Caspari, Charles E., calls attention to “the extremely unsatisfactory method retained in the pharmacopœia for determining the percentage of chlorides in bromides. By the present official method only the most careful and experienced analytical chemist can hope to obtain accurate results, and even he will frequently make an error amounting to 25 per cent of the actual amount of chloride present. If the chloride must be titrated with the bromide by means of a silver solution, then it is much more accurate to add an excess of the silver solution and determine the excess of silver nitrate by means of a standard solution of sulphocyanide, because the end point in this case is much more easily recognized than when potassium chromate is used as an indicator. By far the best method of making the determination consists in treating the mixture of chloride and bromide in acid solution with some oxidizing agent, such as ammonium persulphate or lead peroxide, which will oxidize the hydrobromic acid, but which will not affect the hydrochloric acid, which, after the removal of all bromine, can be titrated with a silver solution. This latter method can be carried out just as expeditiously as the present official method, with very much less chance of error, and it requires but about half an hour to make the entire determination.”—*Meyer Bros. Druggist*, 1905, v. 26, p. 248.

Jones (*Chem. News*, v. 89, p. 229) found that primary ammonium carbonate solution gives a sharp separation of silver chloride from silver bromide.—*Abstract J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 1347.

Planés, Paul, outlines a colorimetric method for the estimation of chlorine and bromine by the use of potassium iodide and the liberation of iodine.—*Bull. de Pharm. du Sud-Est*, 1905, v. 10, pp. 281–289.

Beckurts, H., discusses the action of bromine on strychnine and the production of bromostychnine hydrobromide.—*Arch. d. Pharm.*, 1905, v. 243, p. 493.

Sprattling (*Med. Rec.*, N. Y., Sept. 2, 1905) discusses the abuse of bromides in epilepsy and reports analyzing twenty-seven “patent” nostrums for epilepsy. The basis of all, without exception, was bromide of potassium.—*Abstr. J. Am. M. Ass.*, Chicago, 1905, v. 45, p. 873.

CHLORATES AND BROMATES.

Scholtz, M., outlines a method for the titrimetric estimation of chlorates and bromates by reducing with nitric acid and nitrites and titrating with silver nitrate.—Arch. d. Pharm., Berlin, 1905, v. 243, p. 353.

Jannasch and Jahn discuss the several methods that have been recommended for the reduction of bromates and chlorates, and record experiments with nitric acid, hydrogen peroxide, hydrazin sulphate, formic acid, and hydroxylamin sulphate.—Ber. d. deutsch. chem. Gesellsch., 1905, v. 38, pp. 1576–1589.

COBALT.

Kebler, Lyman F., reports finding cobalt nitrate contaminated with sodium chloride and calcium sulphate.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 183.

FEHLING'S SOLUTION.

Lavalle, F. P., obviates the possible difficulty of recognizing the end reactions with sugar and Fehling's solution by proceeding as follows:

Into a porcelain vessel holding about 200 cc. place 5 or 10 cc. of Fehling's solution, 30 cc. of caustic soda solution (1:3), and 50 or 60 cc. of distilled water; heat, and when the fluid begins to boil add gradually some of the solution of sugar, whose percentage is to be determined. The operation is finished as soon as the last drop causes the blue color of the Fehling's solution to disappear.—Chem. News, Lond., 1905, v. 91, p. 299.

Mrazsek, F. M., quotes Hehner (Chem. Centralbl., 1879, p. 406) in support of his statement that an excess of alkali should be avoided.—*Ibid.*, 1905, v. 92, p. 20.

Van Dormail, J., enumerates several methods in which Fehling's solution has been used, and discusses the element of error that has been demonstrated to exist in the weighing of the resulting oxide of copper.—Ann. de pharm. de Louvain, 1905, v. 11, pp. 281–289.

HALOIDS.

Wentzki, O., discusses the separation of iodine, chlorine, and bromine from one another in mixtures of chlorides, bromides, and iodides.—Zeitschr. f. angew. Chem., 1905, v. 18, pp. 696–698.

Thilo, E. (Chem. Zeit., v. 27, p. 866), points out that when silver nitrate is added to a mixture of chlorides, bromides, and iodides, precipitation occurs in three stages. He proposes to take advantage of this fact, and outlines a method of procedure for the determination of iodides in the presence of bromides and chlorides.—Abstr. Analyst, Lond., 1905, v. 30, p. 69.

Merck, Bernhard, contributes two short papers discussing some of the reactions of iodides with persulphates, and outlining a method for demonstrating the presence of an iodide in a dry way.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 1022.

Margosches, B. M., discusses the use of benzol as an indicator and reviews the literature to demonstrate that Schwezow was not the first to suggest the use of either benzol or toluol.—*Zeitschr. f. Analyt. Chem.*, 1905, v. 44, pp. 392-395.

Pouchet (*Bullet. d. l'Acad. d. méd.*, Paris) reports some historical investigation, personal experimentation, and clinical research bearing on the action of iodides on the circulation.—*Abstr. J. Am. M. Ass.*, Chicago, 1906, v. 46, p. 390.

NITRATES AND NITROGEN.

Busch, E., has prepared synthetic diphenyl-endalino-dihydro-triazol (nitron), which he recommends as an excellent reagent for nitrates in aqueous solution. He asserts that it is sensitive to 1:80,000 of nitric acid. The substance can also be used as a quantitative test.—*Pharm. Post*, Wien, 1905, v. 38, p. 777.

Bay, I. (*Compt. rend.*, Paris, 1905, v. 140, pp. 796-797), discusses the reaction of diphenylamine with nitric acid, and points out that what has been considered as being a characteristic reaction for nitric acid is also produced by oxidizing diphenylamine by other oxidizing agents. It is pointed out that in general all aromatic amines give rise to more or less highly colored oxidation products.—*Abstr. J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 458.

Alvarez, E. P. (*Chem. News*, 1905, v. 91, p. 155), employs a sulphuric acid solution of diphenylamine with resorcinol or betanaphthol, as the colorations obtained are more persistent and are more easily distinguished from one another than when diphenylamine is used alone. He gives detailed directions for preparing the solutions and outlines the method of procedure.—*Abstr. Analyst*, Lond., 1905, v. 30, p. 220.

Hinrichs, G., is quoted as suggesting that the misinterpretation of the color reaction with diphenylamine may be obviated by applying the diphenylamine test for other oxidizing agents first by means of a solution of the former in concentrated hydrochloric acid.—*Abstr. Pharm. Ztg.*, Berlin, 1905, v. 50, p. 928.

Andrews, Lancelot W., points out that the reaction for nitrates with phenolsulphuric acid mixture produces *o*-nitrophenol *p*-sulphonic acid, and not picric acid as assumed by Sprengel or dinitrophenol as suggested by Montenari. (*Ztschr. f. angew. Chem.*, 1905.)—*Abstr. Pharm. Zentralh.*, 1905, v. 46, p. 913.

Lemaitre (*Mon. scient.*, v. 18, p. 253) determined the amount of sodium perchlorate in commercial nitrates by fusing the nitrate

with sodium sulphite and determining the chloride formed by titration with silver nitrate, using a chromate as an indicator, or gravimetrically, the sulphate being first removed with barium nitrate.—*Abstr. J. Am. Chem. Soc., N. Y., 1905, v. 27, p. 1347.*

An abstract from the *Chemiker Zeitung* calls attention to the property of ceric salts, in solution, being decolorized by alkali nitrites without the evolution of gas. The reaction is said to be quantitative and to take place rapidly at ordinary temperatures.—*Abstr. J. Soc. Chem. Ind., London, 1905, v. 24, p. 752.*

Barelt and Schonewald (*Wochenschr. f. Brauerei, v. 21, p. 523*) give figures to show the effect of different kinds of glass upon the results in the Kjeldahl determinations, and demonstrate that the effect is considerable.—*Abstr. J. Am. Chem. Soc., N. Y., 1905, v. 27, p. 1348.*

Neuburger, Albert, discusses the several methods now in use to utilize atmospheric nitrogen. He enumerates the production of nitrides, the production of ammonia and of ammonium compounds, the production of cyanides, and the production of the oxides of nitrogen.—*Ztschr. f. angew. Chem., 1905, v. 18, pp. 1761-1766.*

4. BIOLOGIC REMEDIES.

Arnold, L., contributes several papers on the use of the various animal substances—liver, gall, stomach, heart, blood, skin, marrow, bone, horns, hoofs, urine, excrement, saliva, sperm, and testicles—in medicine by the Arabians.—*Bull. de Pharm. du Sud-Est, 1905, v. 10, pp. 348-351 and 508-517.*

Wainwright, J. W. (*Med. Rec., July 29, 1905*), contributes an exhaustive paper on the various glandular and other animal extracts which have lately come into use in therapeutics.—*Abstr. J. Am. M. Ass., Chicago, 1905, v. 45, p. 493.*

Tada, J. (*Jahrbuch d. Kinderheilkunde, Berlin, 1905, v. 41*), contributes a paper on hypertrophy of the thymus.—*Ibid., p. 817.*

RENNIN.

Vanderkleed, Charles E., discourses on the lack of uniformity in the milk coagulating power of commercial rennin powder and the lack of uniformity in the method of testing. He outlines a method depending on the addition of varying quantities of a solution of rennin to a given quantity of milk and noting the time required to produce firm coagulation.—*Proc. Penna. Pharm. Ass., 1905, p. 192.*

ENZYMES AND ENZYME ACTION.

An editorial discusses "The oxidizing ferments or oxydases" and gives a number of references to the recent literature relating to the subject.—*J. Am. M. Ass., Chicago, 1905, v. 45, p. 856.*

Winckel (Pharm. Post, v. 37, p. 598) points out that emulsin, myrosin, rennin, diastase, trypsin, invertin, and ptyalin all give a violet color when treated with vanillin and hydrochloric acid, and this reaction is further suggested as a method for the detection of enzymes generally. The coloration is readily obtained by treating sections of fatty or oily seeds containing enzymes with the above-named reagents.—Abstr., Analyst, Lond., 1905, v. 30, p. 134.

Illoway, H. (Arch. f. Verdauungskr. XI, No. 1), enumerates some simple methods for the quantitative estimation of the gastric secretions.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 664.

Lewis, H. E. (American Medicine, 1905, Aug. 12), makes a contribution to the study of enzyme action and its relation to human metabolism and the development of tuberculosis.—Abstr. *Ibid.*, p. 1707.

Schittenhelm, Alfred, reports some results obtained from the experimental use of an active enzyme solution obtained by precipitating an aqueous extract of spleen with ammonium sulphate, etc.—Abstr. J. Chem. Soc. Lond., 1905, v. 88, part 2, p. 108 (from Zeit. Physiol. Chem.).

Senter, George, reports some studies on enzyme action and the effect of "poisons" on the rate of decomposition of hydrogen peroxide by hæmase. He concludes that at least some enzymes are amphoteric substances. The poisonous action is to be referred in most cases to a formation of compounds with the enzymes which are inactive towards hydrogen peroxide:—(Proc. Royal Soc., v. 74, pp. 201-217.) Abstr., J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 107. Some additional references are included in the abstract.

von Raumer discusses the use of fermentation processes in the analytical laboratory and points out that in connection with several products containing sugar this practically offers the only satisfactory method for estimating the amount of sugar present. He also points out that one of the great difficulties in connection with the use of fermentation for analytical purposes is the scarcity of pure cultures of the several varieties of yeast. The uses of the several varieties of yeast are discussed and their limitations pointed out. The dependence on compressed yeast is warned against.—Ztschr. f. Unters. d. Nahr. u. Genussm., Berlin, 1905, v. 9, pp. 705-726.

Dunlap and Seymour record some historical and experimental observations on enzymes, particularly the enzymes in the resting seeds of linseed, sweet almonds, and *Croton tiglium*, and in germinated seeds.—J. Am. Chem. Soc., N. Y., 1905, v. 27, pp. 935-946.

Dean, Arthur L., presents tabulated results of experiments with germinating seeds of *Phaseolus vulgaris*.—Bot. Gaz., Chicago, 1905, v. 40, pp. 121-134.

5. VEGETABLE DRUGS.

Sayre, L. E., in a series of articles discusses the pharmacognosy of the new pharmacopœia.—Am. Druggist, 1905, v. 47, p. 66.

Brooks, R. O., in discussing practical drug control, suggests that the most practical method for controlling the quality of drugs sold by the retail druggist is for him to be sufficiently proficient in analytical technique and sufficiently well equipped personally to test and vouch for the quality of the important substances that he deals in.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, pp. 422.

Caeser and Loretz, in the introductory to their annual report for 1905, express the belief that the hypothesis that has been advanced that synthetic products will ultimately replace the natural medicaments and herbs has not been well founded. They believe that the steadily increasing sale of plant drugs should serve to dispel the fears that have been expressed that plant drugs will be dispensed with in the near future.—Geschäfts-Bericht v. Caeser & Loretz, i. Halle a. S., 1905, p. 1.

The Ph. Hisp., VII, in the descriptions and requirements, includes with the definition for each drug a suggestion as to the origin or the habitat of the drug itself. Thus, stramonium is defined as being "the leaf of *Datura stramonium* L. Solanacea, growing spontaneously in Spain."

Squill is described as "the bulb of *Urginea Scilla* Baker (*Scilla maritima* L.), common in the southern and other provinces of Spain."

Cubeb is described as "the fruit of *Piper Cubeba* L. (*Cubeba officinalis* Miq.), Piperacea of Java, Borneo, and Sumatra."

Camphor is defined as being "the stearopten from the essential oil of *Cinnamomum Camphora* Nees et Ebermeier (*Laurus Camphora* L.) Lauracea, trees growing in China, Japan, and in the island of Formosa."—Farmacopea Oficial Española, 1905.

The report of the "Inspectors of Pharmacies" contains numerous suggestions on precautions that are to be exercised in the collection of vegetable drugs, the season of the year best suited for the collection of wood, bulb, bark, leaf, flower, and root drugs. Also some suggestions on washing, drying, garbling, and marketing these drugs.—Bull. Soc. roy. Pharm., Bruxelles, 1905, v. 49, pp. 304-305.

Dohme, A. R. L., discusses the variations that have been found in a number of drugs during the past seven years.—Apothecary, Boston, 1905, v. 17, p. 942.

Rusby, H. H., in an address on the adulteration of vegetable drugs, discusses the general problem implied by the term "adulteration."—Merck's Rep., N. Y., 1905, v. 14, p. 211.

Thomas, D. J., in a report of the committee on adulterations, says:

Until such time as a radical change be made in the method of collecting, drugs will continue to come into the market in the same unsatisfactory condition as heretofore.—Proc. Penn. Pharm. Ass., 1905, p. 49.

Weigel, G., in a comprehensive, illustrated article describes the method of packing crude drugs.—*Pharm. Zentralh.*, 1905, v. 46, p. 623.

Weigel, G., discusses the color reactions that have been proposed from time to time. He concludes that while color reactions are valuable, they should not be relied on too implicitly.—*Pharm. Zentralh.*, 1905, v. 46, p. 921.

Kebler, Lyman F., discusses the organization and working of the drug laboratory.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 79–83.

Kebler, Lyman F., outlines a method for the sampling of drugs and medicines.—*Ibid.*, pp. 348–354.

True, R. H., reports on the drug-plant investigations that have been made in the United States Department of Agriculture.—*Ibid.*, pp. 272–275.

Henkel, Alice, has compiled a comprehensive list of the medicinal plants of the United States that were found enumerated in the trade lists of the larger drug dealers.—*Bul. No. 89, Bur. Plant Ind., Dept. Agric.*, 1906, pp. 76.

Hood, C. S., discusses a number of problems in connection with various drug plants, the origin of a number of indigenous drugs, and the need for their cultivation.—*West. Drug.*, Chicago, 1905, v. 27, pp. 773–776; also, *Proc. Vt. Pharm. Ass.*, 1905, pp. 61–73.

Peckolt, H., enumerates the various plants indigenous to Brazil.—*Ber. d. pharm. Gesellsch.*, Berlin, 1905, v. 15, p. 183.

Day, W. B., enumerates the medicinal plants found in the vicinity of Chicago.—*West. Drug.*, Chicago, 1905, v. 27, pp. 488–489.

Tester, G. A., reviews the medicinal drugs growing in Canada.—*Canad. Drug.*, 1905, v. 17, p. 494.

Long, J., contributes a list of drugs formerly grown by the Shakers at Union Village, Ohio.—*Pharm. Era*, 1905, v. 34, p. 28.

Some editorial comments on the experiments that have been made in connection with the cultivation of vegetable drugs.—*Ibid.*, pp. 51, 384, and 504.

Holmes, E. M., discusses the cultivation of medicinal plants in gardens.—*Pharm. J. Lond.*, 1905, v. 21, p. 474.

Byla discusses the therapeutic results obtained by the use of a new class of remedies, the method of making of which the author promises to contribute to the proceedings.—*Bull. Soc. roy. Pharm. de Bruxelles*, 1905, v. 49, p. 285.

1. CONSTITUENTS.

Chemineau, M. B., in a contribution from the laboratory of materia medica of the L'Ecole Sup. de Paris, discusses the localization of glucosides in plants.—*Abstr. Pharm. J. Lond.*, 1905, v. 21, p. 195.

Tschirch, A. (*Pharm. Post*), discusses the oxymethylantraquinone drugs and their assay.—*Abstr.*, *ibid.*, p. 225.

Christofoletti (Pharm. Zentralh., v. 45, p. 725), reviews Tschirch's method for the determination of oxymethylantraquinone and suggests a modification of the process for the examination of aloes.—Abstr. Year Book, Pharm., Lond., 1905, p. 123.

Caeser and Loretz include a number of suggestions on the composition and the methods for estimating the value of drugs.—Geschäfts Bericht v. Caeser & Loretz, i. Halle a. S., 1905, p. 1.

An unsigned article reviews several of the papers that have recently appeared bearing on the quantitative estimation of tannin and tannin-like substances in drugs and galenical preparations.—Pharm. Prax., 1905, v. 4, pp. 291–300.

ALKALOIDS.

Pictet, Aimé, in an exhaustive study on the origin of alkaloids in plants (originally published in Arch. des sc. phys. et nat., v. 19, p. 329, ff) presents a number of observations and facts and in conclusion paraphrases his findings as follows:

(1) Alkaloids are N-containing extracts of plant cells, which result from the decomposition of complicated bodies.

(2) They frequently undergo chemical change in that they condense with other plant products.

(3) The most frequent change of this kind is methylation, which is produced by means of the formaldehyde derived from the green plant.

(4) The alkaloids with a pyrrolidin or an indol nucleus are derived from a partial decomposition of albumenoid materials.

(5) The same is true of alkaloids containing the pyridin, piperidin, or chinol nucleus, with the exception that these nuclei are not contained in the albumen molecule itself. They are formed after previous methylation through a change in the indol or pyrrol nucleus.—Pharm. Post, Wien., 1905, v. 38, p. 782; also Pharm. Ztg. Berlin, 1905, v. 50, p. 896.

Feldhaus, Julius, records a comparative study of the alkaloid content of the several parts of the stramonium plant, under varying conditions.—Arch. d. Phar., Berlin, 1905, v. 243, p. 328.

Kircher, Adolph, records some observations on the alkaloids of several varieties of datura. The report includes a description of the methods that were followed and a detailed account of the material.—*Ibid.*, p. 309.

Schmidt, Ernst, records a study of the mydriatic solanaceous alkaloids, including an introduction by the author himself and reports on studies of the alkaloids of *Datura metel*, *Datura arborea*, *Datura quercifolia*, *Datura stramonium*, and *Atropa belladonna*, made with the collaboration of several students.—*Ibid.*, p. 303.

He also reports on the examination of the mydriatic alkaloids of the seeds of *Datura alba*.—Apoth. Ztg., Berlin, 1905, v. 20, p. 669.

Kobert, R., publishes a table of the alkaloids of the solanacea, giving the chemical formula, the action on the eye, and the derivation or occurrence.—Riedel's *Berichte*, 1905, p. 11.

Göszling, W., discusses the alkaloids belonging to the phenanthren group, their composition, derivatives, and uses. He also presents a descriptive study of the alkaloids belonging to the purin group, their composition, derivatives, and uses.—*Apoth. Ztg.*, Berlin, 1905, v. 20, pp. 969, 1017.

Leger (*J. Pharm. Chim.*, v. 19, pp. 329 and 479) presents two articles giving the results of investigations upon the root bark of pomegranate, upon coca, belladonna, nux vomica, ignatia bean, ipecac, and Peruvian bark.—Reference in *J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 1342.

Reichard presents nine articles on investigations covering the reactions of morphine, cocaine, atropine, strychnine, brucine, and anti-pyrine.—(*Chem. Ztg.*, v. 28, pp. 299, 339, 912, 977, 1048, 1102; *Pharm. Ztg.*, v. 49, pp. 523, 855; *Pharm Zentralh.* v. 45, p. 645); reference from *J. Am. Chem. Soc.*, N. Y., 1905, v. 27, p. 1342.

Reichard, C., gives a comprehensive review of the reactions that are applicable or characteristic for caffeine and theobromine.—*Pharm. Zentralh.*, 1905, v. 46, p. 846.

Robertson, T. B. (*Univ. of California Public. Physiol.*, 1905, v. 2, pp. 159–162), publishes some observations on the action between the proteid molecule and the ion during the formation of an ion-proteid on the simple addition of the ion to the proteid molecule.—*Biochem. Centralbl.*, 1905, v. 4, p. 544.

Feder, E., discusses the influences of alkaloids on certain processes of oxidation.—(*Arch. Pharm.*, v. 242, pp. 680–704.) *J. Chem. Soc. Lond.*, 1905, v. 88, p. 151.

Lutz, L. (*Bul. Soc. Bot. France*, 1905, v. 52, pp. 194–202), in an article on the assimilation of organic nitrogenous substances by plants, concludes that alkaloids, in common with ammonia compounds and pyridin bases, are not directly assimilable but that they may become available in the presence of some form of assimilable nitrogen.—*Exp. Sta. Rec.*, v. 17, No. 4, p. 348.

2. MICROSCOPICAL DESCRIPTIONS.

Sayre, L. E., in a review of the pharmacognosy of the new U. S. P., says:

It is unfortunate that space in the U. S. P. would not admit of any lengthy microscopical descriptions of drugs, but it is well to note that an entering wedge has been made for these descriptions in a very few cases. It is seldom we find described in the text of the Pharmacopœia any anatomical structures where the compound microscope is necessary for verification. A phrase here and there is employed; more of them might have been injected into the text to the advantage of the U. S. P.—*Am. Druggist*, N. Y., 1905, v. 47, p. 66.

Whelpley, Henry M., calls attention to the fact that the new pharmacopœia directs the use of the microscope in determining the quality and identity of certain drugs and chemicals. An extended knowledge of the constitution of powdered drugs is not required, the chief object being to exclude certain common adulterants. Whelpley predicts that the time is coming when the microscope will be in every drug store as it is now in every physician's office.—Proc. Missouri Pharm. Ass., 1905, p. 60.

6. PHARMACEUTICAL PREPARATIONS.

Wilbert, M. I., calls attention to the changes that have been made in connection with the preparation of several official tinctures and wines.—Am. J. Pharm., Phila., 1905, v. 77, p. 365.

Zeig, A. C., discusses the manufacture of pharmaceutical preparations in a general way.—Am. Druggist, N. Y., 1905, v. 47, p. 28.

Caldwell, Paul, discusses some familiar preparations.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 220.

Piehler, J., describes and figures an apparatus that is designed to facilitate the making of chocolate pastilles.—Apoth. Ztg., Berlin, 1905, v. 20, p. 858.

Scholtz, M., discourses on the relations existing between chemical research and pharmaceutical practices.—*Ibid.*, p. 731.

An editorial in the New York Medical Journal comments on the address read by E. H. Gane at the Atlantic City meeting of the American Pharmaceutical Association, in which he directs attention to the need for so shaping pharmaceutical research as to bring it more in line with the practical needs of the business pharmacists. As an illustration of this need Gane points out that the revisers of the pharmacopœia have taken cognizance of the advances that have been made in chemistry, botany, and pharmacology, but that the book itself does not reflect the progress that has been made in galenical pharmacy.—N. Y. Med. J., 1905, v. 82, p. 543.

1. DECOMPOSITION OF PREPARATIONS.

Schoorl and van den Berg discuss the influences of air and light on chloroform, bromoform, iodoform, and chloral hydrate.—Ber. d. pharm. Gesellsch., Berlin, 1905, v. 15, pp. 386 and 419.

2. INCOMPATIBILITY.

Planes, P. (Bull. de Pharm. du Sud-Est.), points out that a mixture of boric acid and sodium salicylate becomes moist and unsuitable for use as a powder, probably due to combination, with elimination of water and the formation of a sodium boro-salicylate.—Abstr. Pharm. J., Lond., 1905, v. 21, p. 869.

Devalmont (Oesterr. Zeitschr. f. Pharm., 1905) points out that the following solid substances have a tendency to liquefy, or at least to soften, when brought together: Acetanilide with chloral; antipyrine with betanaphthol, sodium salicylate, phenol, salol, urethane; acetanilide with menthol, thymol, resorcin; betanaphthol with antipyrine, camphor, phenol, menthol; camphor with betanaphthol, sodium salicylate, phenol, salol, urethane; phenacetin with betanaphthol, hydrated chloral, phenol; salicylic acid with exalgin, phenol, menthol.—Abstr. Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, pp. 142.

Lyons, A. B. (Pharm. Review, v. 22, p. 365), recounts a number of experiments relating to the incompatibilities of some quinine salts.—Am. Druggist, 1905, v. 47, p. 270.

3. GALENICALS.

Hill, Charles Alexander, points out that useful as the solid content factor undoubtedly is to the manufacturer, as an official standard it is easily overvalued. He adds:

No amount of regulation alone will suffice to make a good galenical preparation, for the production of which there are two requisites—first, a conscience, and second, the ability to make the preparation.—Pharm. J. Lond., 1905, v. 21, p. 92.

“Gnomon” comments on the risks of standardization.—*Ibid.*, p. 114. Naylor, W. A. H., in discussing the standardization of galenicals, says:

The aim should be to produce preparations that will represent the sum total of therapeutic activity of the drugs operated upon except in cases where it is desired to obtain the medicinal effect of definite principles, the physiological action of which is indisputable.

He also cautions against the dependence on standardized drugs, pointing out that until a series of experiments with various standardized drugs definitely demonstrates that the official processes extract a definite proportion of the alkaloid it is certainly unwise to rely on drugs of standard strength for the preparation of galenicals unless the final product is also assayed.—*Ibid.*, pp. 123–127.

Editorial comments on the papers by Hill and Naylor discuss some of the additional points and suggest that:

There is need to hasten slowly. A great danger lies in the tendency to recommend official standards prematurely. * * * The cause of pharmacy will not be furthered by the hasty adoption of standards for all manner of drugs with regard to which pharmacologists are still in the darkness of ignorance or doubt, even if it is admitted that in addition to therapeutic uniformity, a uniformity of physical characteristics is also in some degree desirable. * * *—*Ibid.*, p. 111.

v. Kazay, Endre, describes a device and a method of photometric estimation by means of which he believes it to be possible to determine

not alone the activity, but also the concentration of galenical preparations.—*Pharm. Post*, Wien, 1905, v. 38, p. 775.

MacEwan, Peter, in a review of the U. S. P., says:

Of analysis, purity, assaying, nomenclature, posology, therapeutics, and what not, there is enough and to spare; but galenical pharmacy is conspicuous by its subordinate position. Four dozen preparations new to the book have been added and formulas for six dozen or so have been removed.—*Am. Druggist*, N. Y., 1905, v. 47, p. 95.

Gadd, H. W. & S. C. (*Pharm. J. Lond.*, v. 20, p. 435), in a study of commercial samples of official galenicals present a tabulated summary of wholesale products, extending over five years.—*Year Book Pharm.*, Lond., 1905, pp. 273–274.

Simms, G. G. C., criticises the methods that are followed and the lack of care that is manifested in the keeping of galenical preparations.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 389–391.

Fisk, Frank E., presents short methods for making some of the official preparations.—*Ibid.*, pp. 392–396.

Caldwell, Paul, presents an approximate estimate of the cost per pint or pound of official preparations.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 382.

4. PERCOLATION.

MacEwan, Peter, asserts that—

The most striking feature in the new pharmacopœia is the blow which it strikes at percolation. Not a severe blow, but sufficient to arrest the thoughtful among pharmacists. We have been apt to regard percolation as the surest method of extracting the soluble constituents of drugs, and the idea has carried us beyond the limits of safety in some cases. So I welcome the macero-shaking process which has been adopted in the majority of the assay processes and with at least some of the now official tinctures.—*Am. Druggist*, N. Y., 1905, v. 47, p. 95.

Katz, J. (*Pharm. Zentralh.*, 1905, p. 486), points out that for the production of alcoholic tinctures the process of percolation is the more generally desirable as it is possible to comply more readily with the fundamental requirement for quantitative extraction.—*Chem. Repert. Cöthen*, 1905, p. 200.

Williams, John K., has obtained the best results with the least labor, when the manufacture of tinctures of gummy resinous drugs is conducted upon the plan of remaceration rather than by percolation.—*Proc. Conn. Pharm. Ass.*, 1905, p. 49.

Smith, Henry D., presents a few suggestions on percolation in connection with which he describes and figures a percolating stand.—*Apothecary*, Boston, 1905, v. 17, p. 521.

Gordin, H. M., describes a simple arrangement for percolation with hot alcohol.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 387–388.

5. THE PRODUCTION OF EXTRACTS AND TINCTURES.

An editorial discusses the extract content of official (German) tinctures and fluid extracts, and points out that the pharmacopœia has repeatedly been criticised for not including limitations, particularly minimum limitations based on the systematic work that has been done by E. Dietrich.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 886.

Dohme, A. R. L., makes a comparison of the several advantages that are claimed for acetic acid and for alcohol and concludes that the fact that all of the larger manufacturers are a unit against the use of acetic acid as a menstruum is suggestive of its lack of usefulness or merit.—*West. Druggist*, Chicago, 1905, v. 27, p. 495.

Arends, G., discusses some of the innovations that have been proposed both as to the method of procedure as well as menstruum and concludes that each extract and each tincture must be studied individually and the method of procedure and the menstruum best adapted for the particular drug and preparation adopted.—*Schweiz. Wehnschr. f. Chem. u. Pharm.*, 1905, v. 43, p. 395.

A controversy on the preparation of extracts without evaporation by means of pressure maceration is recorded in the pages of the *Pharmazeutische Zentralhalle*, the contributors and contributions are:

Katz, J.—*Pharm. Zentrallh.* 1905, v. 46, p. 459.

Bruns, W.—*Ibid.*, pp. 543, 659, 676.

Herzog, J.—*Ibid.*, p. 588.

6. STERILIZATION.

Vandermeulen, A., discusses the application of the principles of sterilization to pharmaceutical products and in pharmacy generally. The author discourses on micro-organisms, infection by micro-organisms, the action of heat on bacteria, the sterilization by means of chemicals, and the sterilization by means of physical agents.—*Ann. de Pharm. d. Louvain*, 1905, v. 11, pp. 137-149, 191-197, 232-245, 291-295.

Schoofs, in a lecture on the value and the uses of sterilization, points out the difference between disinfection and sterilization. "Disinfection," he says, "paralyzes the micro-organisms while sterilization destroys them absolutely."—*J. de Pharm., d'Anvers*, 1905, v. 61, pp. 285-286.

Hallberg, C. S. N., discourses on pasteurization and sterilization. He considers boiling as a preservative; sterilization; fallacy regarding distilled water.—*West. Drug.*, Chicago, 1905, v. 27, p. 635.

Baroni, E., discusses the sterilization of hypodermic solutions.—*Boll. Chim. Farm.*, Milan, 1905, v. 44, pp. 273-275.

Gothignes (*Apoth. Ztg.*, v. 20, p. 558) finds that sterilization obtained by burning off with alcohol is very incomplete.—*Abstr. in Merck's Rep.*, N. Y., 1905, v. 14, p. 279.

Green, C. L. (Brit. Med. J., 1905), records comparative experiments with aqueous solutions of antiseptics and with spirituous solutions of the same substances and concludes that the latter are much more efficient for the sterilization of the hands and skin.—Abstr. J. Am. M. Ass., Chicago, 1905, v. 45, p. 1365.

7. FORMS OF ADMINISTRATION.

CACHETS.

An unsigned article, probably an abstract from a trade circular, figures and describes an apparatus that is designed to fill and seal the "dry seal" cachet devised by F. Sevcik.—Apoth. Ztg., Berlin, 1905, v. 20, p. 645; Pharm. Ztg., Berlin, 1905, v. 50, p. 695.

The Spanish Pharmacopœia contains a description of rice flour cachets that are to be used for enveloping powdered and massed drugs.—Farmacopea Oficial Española, 1905, p. 160.

Löber, O., figures and describes a self-opening folded paper powder holder or cachet.—Pharm. Post, Wien, 1905, v. 38, p. 722.

CAPSULES.

The Spanish Pharmacopœia contains a description of and formulas for three varieties of gelatin capsules—hard, soft, and medium.—Farmacopea Oficial Española, 1905, p. 161.

The Ph. Ndl., IV, contains the following formulas for gelatin capsules:

Hard gelatin basis for capsules, for copaiba balsam:

Gelatin.....	3
Water.....	6
Glycerin.....	1

Soft gelatin basis, for castor oil capsules:

Gelatin.....	23
Water.....	32
Glycerin.....	45

Heat the gelatin and water in the water bath until the former is dissolved, then add the glycerin.—Year Book Pharm. Lond., 1906, p. 130 (From Pharm. Centralh., 1905).

Unger, E., describes a protein gelatin capsule containing upward of 70 per cent of albumin which he believes to be preferable to the ordinary gelatin capsule, because of its being more readily dissolved in the stomach.—Apoth. Ztg., Berlin, 1905, v. 20, p. 770.

Wendt, Gustav, discusses the article by Unger, quoted above, and controverts the claims made by the former in connection with the protein gelatin capsules recommended.—*Ibid.*, p. 832.

Wilbert, M. I., suggests that a general formula for hypodermic tablets be included in the pharmacopœia.—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 366.

Rodwell, Henry, discusses the preparation of compressed tablets under the general headings: Theobroma emulsion, ether-alcohol emulsion, granulation and cohesion, lubrication and finish, compression and disintegration, compressed lozenges.—*Pharm. J., Lond.*, 1905, v. 21, p. 826. Discussion, *ibid.*, p. 838.

An abstract from a previous article by the same author is published in *Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 229.

Lowry, Wm. J., jr., points out that corn starch made into a paste with hot water and used for the making of different granulations, sometimes plus a little uncooked starch, will materially aid the disintegration of the tablets of even insoluble materials.—*Proc. Md. Pharm. Ass.*, 1905, p. 27; also *Apothecary, Boston*, 1905, v. 17, p. 951.

Löbner, O., figures and describes several new compressing machines for tablets.—*Pharm. Post, Wien*, 1905, v. 38, p. 721.

Thomann (Schweiz. Wchnschr. f. Chem. u. Pharm., 1905) points out the needs for testing and controlling the tablets put out by manufacturing concerns. He reports finding tablets of sodium salicylate that purported to contain 0.25 gramme of sodium salicylate, but weighed 0.25 gramme scant and contained upwards of 15 per cent of talcum. Morphine tablets also showed great variation in the amount of morphine contained in each tablet.—*Pharm. Ztg., Berlin*, 1905, v. 50, p. 561.

Patch, Edgar L., quotes the finding of strychnine, morphine, and calomel tablets without the active ingredients.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 190.

II. INTERNATIONAL STANDARDS.

1. INTERNATIONAL CONFERENCE FOR THE UNIFICATION OF PHARMACOPŒIAL FORMULÆ FOR POTENT MEDICAMENTS (BRUSSELS CONFERENCE).

1. PROJECT FOR AN AGREEMENT RESPECTING THE UNIFICATION OF THE PHARMACOPŒIAL FORMULAS FOR POTENT DRUGS.

The Governments of Great Britain, Germany, Austria and Hungary, Belgium, Bulgaria, Denmark, Spain, the United States of America, France, Greece, Italy, the Grand Duchy of Luxemburg, Norway, the Netherlands, Portugal, Russia, Servia, Sweden, and Switzerland, having recognized the utility of concluding an agreement with a view to the unification of the pharmacopœial formulas for potent drugs on the basis indicated in the final protocol signed on the 20th September, 1902, as a result of the conference held at Brussels, the undersigned, duly authorized thereto, have agreed upon the following stipulations:

ARTICLE 1.—The medicinal substances inscribed in the table given below shall be designated, in the pharmacopœia published by each of the contracting Governments, by the Latin names employed in this table, and shall conform with the directions indicated in the column opposite.

Latin names and synonyms of drugs and preparations.	Pharmaceutical directions.
Aconitum Napellus. L.....	
Aconiti tuber seu Tuber Aconiti.....	Use only the tuber of the current year, dried. Powdered drug to be used entire, without separation of residue.
Aconiti tinctura seu Tinctura Aconiti.....	Prepare by percolation with alcohol (70 per cent. by volume). Tincture to be standardized to 0.05 per cent of total alkaloids.
Atropa Belladonna. L.....	
Belladonnæ folium seu Folium Belladonnæ.....	Use only the leaf, dried. Powdered drug to be used entire.
Belladonnæ tinctura seu Tinctura Belladonnæ....	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
Belladonnæ extractum seu Extractum Belladonnæ.	Prepare a solid extract (containing about 10 per cent of water) by means of alcohol (70 per cent).
Colchicum autumnale. L.....	
Colchici semën seu Semen Colchici.....	Use only the seed.
Colchici tinctura seu Tinctura Colchici.....	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
Digitalis purpurea. L.....	

Latin names and synonyms of drugs and preparations.	Pharmaceutical directions.
<i>Digitalis folium</i> seu <i>Folium Digitalis</i>	Use the leaf of the second year. Powdered drug to be used entire.
<i>Digitalis tinctura</i> seu <i>Tinctura Digitalis</i>	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
<i>Uragoga Ipecacuanha</i> . <i>Baill</i>	
<i>Ipecacuanhæ radix</i> seu <i>Radix Ipecacuanhæ</i>	Powder only the root-bark, rejecting the woody portion. The powder should have an alkaloidal strength of 2 per cent.
<i>Ipecacuanhæ tinctura</i> seu <i>Tinctura Ipecacuanhæ</i> ..	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
<i>Ipecacuanhæ sirupus</i> seu <i>Sirupus Ipecacuanhæ</i>	Prepare with 10 per cent of the tincture.
<i>Hyoscyamus niger</i> . <i>L</i>	
<i>Hyoscyami folium</i> seu <i>Folium Hyoscyami</i>	Use only the leaf.
<i>Hyoscyami tinctura</i> seu <i>Tinctura Hyoscyami</i>	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
<i>Hyoscyami extractum</i> seu <i>Extractum Hyoscyami</i> .	Prepare a solid extract (containing about 10 per cent of water) by means of alcohol (70 per cent).
<i>Strychnos Nux vomica</i> . <i>L</i>	
<i>Strychni semen</i> seu <i>Semen Strychni</i> seu <i>Nux vomica</i> .	Alkaloidal strength (of powdered drug) 2.5 per cent.
<i>Strychni tinctura</i> seu <i>Tinctura Strychni</i> ; <i>Nucis vomicæ tinctura</i> seu <i>Tinctura Nucis vomicæ</i> .	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent). Alkaloidal strength 0.25 per cent.
<i>Strychni extractum</i> seu <i>Extractum Strychni</i> ; <i>Nucis vomicæ extractum</i> seu <i>Extractum Nucis vomicæ</i> .	Prepare by means of alcohol (70 per cent). Alkaloidal strength 16 per cent.
<i>Opii pulvis</i> seu <i>Pulvis Opii</i>	Powder to be dried at 60° C. Strength in morphine 10 per cent.
<i>Opii extractum</i> seu <i>Extractum Opii</i>	Strength in morphine 20 per cent.
<i>Opii tinctura</i> seu <i>Tinctura Opii</i>	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent). Strength in morphine 1 per cent.
<i>Opii tinctura crocata</i> seu <i>Tinctura Opii crocata</i> seu <i>Laudanum Sydenhami</i> .	Strength in morphine 1 per cent.
<i>Opii et Ipecacuanhæ pulvis compositus</i> seu <i>Pulvis Doveri</i> .	To contain 10 per cent of <i>Pulvis Opii</i> .
<i>Opii tinctura benzoicæ</i> seu <i>Tinctura Opii benzoicæ</i> .	Strength in morphine 0.05 per cent.
<i>Strophanthi tinctura</i> seu <i>Tinctura Strophanthi</i>	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent). Seeds not to be freed from fat.
<i>Sclerotium clavicipitis purpuræ Tul.</i> seu <i>Clavicipitis purpuræ Tul.</i> <i>Sclerotium</i> .	
<i>Secale cornutum</i> seu <i>Ergotum Secale</i>	Ergot to be not more than one year old and kept whole.
<i>Secalis cornuti extractum</i> seu <i>Extractum Secalis Cornuti</i> ; <i>Ergoti extractum</i> seu <i>Extractum Ergoti</i> .	Prepare a watery extract and make up with alcohol (60 per cent).
<i>Secalis cornuti extractum fluidum</i> seu <i>Extractum fluidum Secalis cornuti</i> ; <i>Ergoti extractum fluidum</i> seu <i>Extractum fluidum Ergoti</i> .	Strength 100 per cent.
<i>Acidum hydrocyanicum dilutum</i>	Strength 2 per cent.
<i>Laurocerasi aqua</i> seu <i>Aqua Laurocerasi</i>	Strength 0.10 per cent.
<i>Amygdalæ amaræ aqua</i> seu <i>Aqua Amygdalæ amaræ</i> .	Strength 0.10 per cent.
<i>Phenoli solutio</i> seu <i>Aqua phenolata</i>	Strength 2 per cent.
<i>Arsenas sodii</i> seu <i>Sodii arsenas</i> ; <i>Arsenicicum natrium</i> seu <i>Natrium arsenicicum</i> .	The crystallized salt, containing 36.85 per cent of arsenic acid.

Latin names and synonyms of drugs and preparations.	Pharmaceutical directions.
Arsenicalis liquor Fowleri seu Liquor arsenicalis; Fowleri seu Kalii arsenicosi liquor.	Strength in arsenious acid 1 per cent.
Ferri iodidi sirupus seu Sirupus iodeti ferrosi seu Sirupus ferri iodati.	Strength in anhydrous ferrous iodide 5 per cent.
Cantharidis tinctura seu Tinctura Cantharidis.....	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
Iodi tinctura seu Tinctura iodi.....	Strength 10 per cent. Prepare with alcohol (95 per cent).
Lobeliæ tinctura seu Tinctura Lobeliæ.....	Strength 10 per cent. Prepare by percolation with alcohol (70 per cent).
Cocainum hydrochloricum.....	The anhydrous salt.
Hydrargyri unguentum seu Unguentum Hydrargyri.	Strength 30 per cent.
Antimoniale vinum seu Vinum antimoniale; Stibiatum vinum seu Vinum stibiatum.	Strength in tartar emetic 0.40 per cent.

ART. 2.—So far as regards substances other than those which appear in the Table contained in Article 1, and which may hereafter be included in the Pharmacopœias, the Contracting Governments undertake that the following rules shall apply:

(a) No potent drug shall be directed to be prepared in the form of a medicinal wine (*vinum*);

(b) Tinctures of potent drugs shall be directed to be prepared of the strength of 10 per cent and by percolation.

(c) Fluid extracts of potent drugs shall be prepared of the strength of 100 per cent.

ART. 3.—The Contracting Governments shall adopt a normal drop measure, the external diameter of whose outlet tube shall be exactly 3 millimeters, that is to say, which, at a temperature of 15 degrees Centigrade, and with distilled water, shall yield 20 drops to the gramme.

ART. 4.—Governments which have not taken part in the present agreement shall be allowed at their own request to signify their adhesion to it. Such adhesion shall be notified, through the proper diplomatic channel, to the Belgian Government, and by it to the other Signatory Governments.

ART. 5.—The present agreement shall come into force one month after the date of its signature. It is understood, nevertheless, that the stipulations of articles 1, 2, and 3 shall not become binding upon any one of the Contracting Parties until the publication of a new issue, or of a supplement, of its pharmacopœia.

ART. 6.—In case one or other of the Contracting Parties shall denounce the present agreement, such denunciation shall take effect only so far as regards itself, and then only six months after the day upon which such denunciation shall have been notified to the Belgian Government.

PROCÈS-VERBAL OF SIGNATURE.

The undersigned, duly authorized, have met together on the 29th November, 1906, at the Belgian ministry for foreign affairs, in order to proceed to the signature of the act intended to give diplomatic sanction to the resolutions adopted by the conference which assembled at Brussels in the month of Sep-

tember, 1902, with a view to the unification of the pharmacopœial formulas for potent drugs.

At the moment of affixing their signatures to the said act, the representatives of Germany, Austria-Hungary, the United States of America, Great Britain, Portugal, and Sweden have formulated, in the name of their respective Governments, the following reservations:

I. *Reservations formulated by the German Government.*^a—The Imperial Government does not impose upon itself, by the fact of signing the present agreement, any other obligation beyond that of exercising its influence, when the proper time arrives—that is to say, at the date of the next revision of the German Pharmacopœia—in order to bring the latter into conformity with the present agreement.

At the same time the Imperial Government reserves to itself the right of introducing into the stipulations of this agreement any modifications which, on the one hand, appear necessary in order to take account of the progress of medical and pharmaceutical science, and which, on the other hand, may be desirable from the point of view of the unification of the German Pharmacopœia.

II. *Reservations formulated by the Austrian Government.*—So far as regards *opii pulvis* the Austrian Government reserves to itself the right of permitting the sale of the pure drug containing, as a maximum, 12 per cent. of morphine.

III. *Reservations formulated by the Government of the United States of America.*—The Government of the United States does not assume, by the fact of signing the present agreement, any other obligation beyond that of exercising its influence in order that, at the next revision of the American Pharmacopœia, the latter may be brought into harmony with the said agreement.

IV. *Reservations formulated by the Government of His Britannic Majesty.*—The Government of His Britannic Majesty declares that it reserves the right of introducing into the stipulations of the present agreement such modifications in detail as the progress of medical and pharmaceutical science may render necessary from time to time.

The Government of His Britannic Majesty further declares that it reserves the right of adhering to the agreement, and of denouncing it, with reference to each of the British colonies or possessions, separately.

V. *Reservations formulated by the Portuguese Government.*—The resolutions of the international conference held at Brussels for the unification of the pharmacopœial formulas of potent drugs shall be applied in Portugal. Nevertheless, the vernacular Portuguese name of each substance shall appear in the text of the pharmacopœia, and shall be adopted as the primary denomination; one of the Latin names inscribed in the table contained in article 1 of the present agreement shall be used as the first synonymous denomination.

VI. *Reservations formulated by the Swedish Government.*—1. The denominations of the potent drugs enumerated in the present agreement, differing entirely from those employed in the Swedish Pharmacopœia, shall not be inscribed in the text itself of that pharmacopœia, but shall appear in a special supplement to the new issue of the pharmacopœia which is in course of preparation;

^a The Government of the Grand Duchy of Luxemburg has declared that Luxemburg, which by arrangement with Germany has adopted the German Pharmacopœia, has signed the agreement under the reservations formulated by the German Government.

2. The denomination of the medicinal wine *vinum glycyrrhizae opiatum* shall be maintained in Sweden;

3. As the preparation of tinctures of drugs by percolation involves an increase in the price of these products, this method seems not altogether suitable for employment in a general manner.

At the moment of proceeding to the signature of the present *procès-verbal* the undersigned declare themselves in accord in recognizing that the right referred to in the first reservation formulated by the Government of His Britannic Majesty is acquired by all the Signatory Governments.

It is understood that the Contracting Parties which exercise this right will inform each other, reciprocally, through the intermediary of the Belgian Government, of any modifications introduced into the stipulations of the agreement.

2. COMPARATIVE TABLE SHOWING THE DEGREE OF COMPLIANCE, IN THE SEVERAL PHARMACOPÆIAS PUBLISHED IN 1905, WITH THE PROVISIONS OF THE BRUSSELS CONFERENCE.

	Protocol, International.	U. S. P., VIII.	Ph. Hisp., VII.	Ph. Ndl., IV.
<i>Aconitum napellus</i> (L.):				
Title.....	<i>Aconiti tuber seu Tuber Aconiti</i>	<i>Aconitum</i>	<i>Radix aconiti</i>	<i>Tubera aconiti</i>
Requirement.....	Tuber of the current year.....	Collected in autumn; not less than 0.5 per cent of aconitine.	Origin specified.....	Tuber of the current year; origin specified.
<i>Tinctura aconiti</i> :				
Title.....	<i>Aconiti tinctura seu Tinctura Aconiti</i>	<i>Tinctura aconiti</i>	<i>Tinctura alcoholica aconiti</i>	<i>Tinctura aconiti</i>
Strength.....	10 per cent.....	10 gm. : 100 cc.	Same as P. I.	Same as P. I.
Menstruum.....	Alcohol (70 per cent).....	Alcohol 70, water 30.....	Same as P. I.	Same as P. I.
Requirement.....	0.05 per cent of total alkaloids.....	Aconitine, 0.045 per cent.....	Same as P. I.	Same as P. I.
<i>Atropa belladonna</i> (L.):				
Title.....	<i>Belladonnae folium seu Folium Belladonnae</i>	<i>Belladonnae folia</i>	<i>Folium belladonnae</i>	<i>Folia belladonnae</i>
Requirement.....	Use only the leaf, dried.....	Dried leaves; not less than 0.3 per cent of mydriatic alkaloids.	Dried leaves; origin specified.....	Dried leaves; origin specified; qualitative test for alkaloids.
<i>Tinctura belladonnae</i> :				
Title.....	<i>Belladonnae tinctura seu Tinctura Belladonnae</i>	<i>Tinctura belladonnae foliorum</i> ...	<i>Tinctura alcoholica belladonnae</i> ...	<i>Tinctura belladonnae</i>
Strength.....	10 per cent.....	10 gm. : 100 cc.	Same as P. I.	Same as P. I.
Menstruum.....	Alcohol (70 per cent).....	Diluted alcohol.....	Same as P. I.	Same as P. I.
Requirement.....		100 cc. : 0.03 gm. of alkaloids from belladonna leaves.		Color; sp. gr.; extract; qualitative test for alkaloids.
<i>Extractum belladonnae</i> :				
Title.....	<i>Belladonnae extractum seu Extractum Belladonnae</i>	<i>Extractum belladonnae foliorum</i>		
Requirement.....	Solid extract (containing about 10 per cent of water) made with alcohol (70 per cent).....	Solid extract containing 1.4 per cent of mydriatic alkaloids; made with a mixture of alcohol 2 and water 1.		

2. COMPARATIVE TABLE SHOWING THE DEGREE OF COMPLIANCE, IN THE SEVERAL PHARMACOPŒIAS PUBLISHED IN 1905, WITH THE PROVISIONS OF THE BRUSSELS CONFERENCE—Continued.

	Protocol, International.	U. S. P., VIII.	Ph. Hesp., VII.	Ph. Ndl., IV.
<i>Colegium autumnale</i> (L.):				
Title.....	<i>Colchici semen</i> seu <i>Semen Colchici</i> .	<i>Colchici semen</i>	<i>Seimen colchici</i>	<i>Seimen colchici</i> .
Requirement.....	Use only the seed.	The seed; not less than 0.45 per cent of colchicine.	The seed; origin specified.....	The ripe seed; should not be kept longer than one year.
<i>Tinctura colchici</i> :				
Title.....	<i>Colchici tinctura</i> seu <i>Tinctura Colchici</i> .	<i>Tinctura colchici seminis</i>	<i>Tinctura alcoholica colchici</i>	<i>Tinctura colchici</i> .
Strength.....	10 per cent.....	10 gm.: 100 cc.....	Same as P. I.....	Same as P. I.
Menstruum.....	Alcohol (70 per cent).....	Alcohol 60, water 40.....	Same as P. I.....	Same as P. I.
Requirement.....		100 cc.: 0.04 gm. of colchicine.		Color; sp. gr.; extract; qualitative test for alkaloid.
<i>Digitalis purpurea</i> (L.):				
Title.....	<i>Digitalis folium</i> seu <i>Folium Digitalis</i> .	<i>Digitalis</i>	<i>Folium digitalis</i>	<i>Folia digitalis</i> .
Requirement.....	The leaf of the second year.....	The dried leaves; second year's growth at the commencement of flowering.	Second year's growth; origin specified.	From flowering herb, second year; origin specified.
<i>Tinctura digitalis</i> :				
Title.....	<i>Digitalis tinctura</i> seu <i>Tinctura Digitalis</i> .	<i>Tinctura digitalis</i>	<i>Tinctura alcoholica digitalis</i>	<i>Tinctura digitalis</i> .
Strength.....	10 per cent.....	10 gm.: 100 cc.....	Same as P. I.....	Same as P. I.
Menstruum.....	Alcohol (70 per cent).....	Diluted alcohol.....	Same as P. I.....	Same as P. I.
Requirement.....				Sp. gr.; extract; qualitative test for active principles.
<i>Uragoga ipecacuanhæ</i> (Baill.):				
Title.....	<i>Ipecacuanhæ radix</i> seu <i>Radix Ipecacuanhæ</i> .	<i>Ipecacuanha</i> (Rio or Carthagena).	<i>Radix ipecacuanhæ</i> (Rio only) ...	<i>Radix ipecacuanhæ</i> (Rio).
Requirement.....	Only the root bark to be used. The powder to have an alkaloidal strength of 2.0 per cent.	1.75 per cent of ipecac alkaloids.....	Same as P. I.....	Same as P. I.

Tinctura ipecacuanhæ:					
Title.....	Ipecacuanhæ tinctura seu Tinctura Ipecacuanhæ.	Not official.....	Tinctura alcoholica Ipecacuanhæ.	Tinctura ipecacuanhæ.	
Strength.....	10 per cent.		Same as P. I.	Same as P. I.	
Menstruum.....	Alcohol (70 per cent.)		Same as P. I.	Same as P. I.	
Requirement.....				Color, sp. gr.; extract; qualitative test for alkaloids.	
Syrupus Ipecacuanhæ:					
Title.....	Ipecacuanhæ sirupus seu Sirupus Ipecacuanhæ.	Syrupus Ipecacuanhæ.....	Syrupus Ipecacuanhæ.	Syrupus Ipecacuanhæ.	
Strength.....	10 per cent of the tincture.	7 cc. of fluid extract in 100 cc.	Same as P. I.	Same as P. I.	
Title.....	Hyoscyami folium seu Folium Hyoscyami.	Hyoscyamus.....	Hyoscyamus.	Folia hyoscyami	
Requirement.....	Use only the leaf.	Dried leaves and flowering tops, second year; 0.08 per cent of mydriatic alkaloids.	The leaf; origin suggested.	The leaf collected from the flowering herb grown in Holland.	
Tinctura hyoscyami:					
Title.....	Hyoscyami tinctura seu Tinctura Hyoscyami.	Tinctura hyoscyami.....	Tinctura alcoholica hyoscyami.	Tinctura hyoscyami.	
Strength.....	10 per cent.	10 gm. : 100 cc.	Same as P. I.	Same as P. I.	
Menstruum.....	Alcohol (70 per cent.)	Diluted alcohol.	Same as P. I.	Same as P. I.	
Requirement.....		100 cc. : 0.007 gm. of mydriatic alkaloids.		Color, sp. gr.; qualitative test.	
Extractum hyoscyami:					
Title.....	Hyoscyami extractum seu Extractum Hyoscyami.	Extractum hyoscyami.....	Extractum alcoholicum hyoscyami.	Extractum hyoscyami.	
Menstruum.....	Alcohol (70 per cent.)	Alcohol 60, water 40	Same as P. I.	Same as P. I.	
Requirement.....	Solid extract (containing about 10 per cent of water).	0.3 per cent of mydriatic alkaloids.	Same as P. I.	Qualitative tests are appended.	
Strychnos nux vomica (L.):					
Title.....	Strychni semen seu Semen Strychni seu Nux vomica.	Nux vomica.....	Nux vomica seu semen strychni.	Semen strychni; nux vomica.	
Requirement.....	2.5 per cent total alkaloids.	The dried ripe seed; 1.25 per cent of strychnine.	Same as P. I.	Same as P. I.	

2. COMPARATIVE TABLE SHOWING THE DEGREE OF COMPLIANCE, IN THE SEVERAL PHARMACOPŒIAS PUBLISHED IN 1905, WITH THE PROVISIONS OF THE BRUSSELS CONFERENCE—Continued.

	Protocol, International.	U. S. P., VIII.	Ph. Hisp., VII.	Ph. Ndl., IV.
<i>Tinctura nucis vomicæ:</i>				
Title.....	Strychni tinctura seu Tinctura Strychni, Nucis vomicæ-tinctura seu Tinctura Nucis vomicæ, 10 per cent.	Tinctura nucis vomicæ.....	Tinctura alcoholica nucis vomicæ.....	Tinctura strychni.
Strength.....	Alcohol (70 per cent).....	2 gm. extract; 100 cc.....	Same as P. I.....	Same as P. I.
Menstruum.....	0.25 per cent total alkaloids.....	Alcohol 75 cc., water 25 cc.....	Same as P. I.....	Same as P. I.
Requirement.....	Extractum nucis vomicæ:	100 cc.; 0.1 gm. strychnine.....	Same as P. I.....	Same as P. I. and qualitative tests.
Title.....	Strychni extractum seu Extractum Strychni, Nucis vomicæ-tinctura seu Extractum Nucis vomicæ.	Extractum nucis vomicæ.....	Extractum alcoholicum nucis vomicæ.....	Extractum strychni.
Menstruum.....	Alcohol (70 per cent).....	Acetic acid 50 cc., water 130 cc.; made up with alcohol.....	Same as P. I.....	Same as P. I.
Requirement.....	16 per cent total alkaloids.....	Powdered extract; 5 per cent strychnine.....	Same as P. I.....	Same as P. I. and qualitative tests.
Opium:				
Title.....	Opii pulvis seu Pulvis Opii.....	Opii pulvis.....	Pulvis opii.....	Opium.
Requirement.....	Powder to be dried at 60° C.; morphine 10 per cent.	Dried at not exceeding 85° C.; morphine 12 to 12.5 per cent.	Same as P. I.....	Morphine at least 10 per cent.
Extractum opii:				
Title.....	Opii extractum seu Extractum Opii.....	Extractum opii.....	Extractum aquosum opii.....	Extractum opii.
Requirement.....	Morphine 20 per cent.....	Same as P. I.....	Same as P. I.....	Same as P. I.
Tinctura opii:				
Title.....	Opii tinctura seu Tinctura Opii.....	Tinctura opii.....	Tinctura alcoholica opii.....	Tinctura opii.
Strength.....	10 per cent.....	10 gm.; 100 cc.....	5 per cent of extract.....	Same as P. I.
Menstruum.....	Alcohol (70 per cent).....	Diluted alcohol.....	Same as P. I.....	Same as P. I.
Requirement.....	Morphine 1 per cent.....	Morphine 1.2 to 1.25 per cent.....	Same as P. I.....	Same as P. I.; color; taste; sp. gr.; extract.

2. COMPARATIVE TABLE SHOWING THE DEGREE OF COMPLIANCE, IN THE SEVERAL PHARMACOPŒIAS PUBLISHED IN 1905, WITH THE PROVISIONS OF THE BRUSSELS CONFERENCE—Continued.

	Protocol, International.	U. S. P., VIII.	Ph. Hisp., VII.	Ph. Ndl., IV.
Extractum ergotæ: Title.....	Secalis cornuti extractum seu Extractum Secalis Cornuti; Ergoli extractum seu Extractum Ergoli.	Extractum ergotæ.....	Extractum aquosum secalis cornuti.	Extractum secalis cornuti.
Menstruum and requirements	Prepare a watery extract and make up with alcohol (60 per cent).	Hydro-alcoholic extract treated with HCl and neutralized with NaCO ₃ .	Prepare with distilled water; make up with alcohol.	Extract with chloroform water; make up with alcohol.
Fluidextractum ergotæ: Title.....	Secalis cornuti extractum fluidum, seu Extractum fluidum Secalis cornuti; Ergoli extractum fluidum seu Extractum fluidum Ergoli.	Fluidextractum ergotæ.....	Not official.	Extractum secalis cornuti liquidum.
Strength.....	100 per cent.	100 gm. : 100 cc.		Same as P. I.
Menstruum.....		Acetic acid 2, diluted alcohol 98.		Color, sp. gr., extract.
Requirement.....				
Acidum hydrocyanicum dilutum: Title.....	Acidum hydrocyanicum dilutum.	Acidum hydrocyanicum dilutum.	Acidum cyanhydricum medicinale	Acidum hydrocyanicum dilutum.
Requirement.....	Strength, 2 per cent.	Strength 2 per cent in water; directions for keeping.	Strength 2 per cent.	Strength 2 per cent in water 80, alcohol 20.
Aqua laurocerasi: Title.....	Laurocerasi aqua seu Aqua Laurocerasi.	Not official.	Aqua distillata lauro-cerasi	Aqua laurocerasi.
Requirement.....	Strength, 0.10 per cent.		Strength 0.10 per cent of hydrocyanic acid.	Not less than 0.054 per cent of hydrocyanic acid.
Aqua amygdalæ amara: Title.....	Amygdalæ amara aqua seu Aqua Amygdalæ amara.	Aqua amygdalæ amara.	Not official.	
Requirement.....	Strength, 0.10 per cent.	0.10 per cent of oil of bitter almond in distilled water.		

Aqua phenolata:					
Title.....	Phenoli solutio seu Aqua phenolata	Not official.....	Aqua phenicata.....	Solutio phenoli.	
Requirement.....	Strength, 2 per cent.....		Same as P. I.	Same as P. I.	
Sodii arsenas:					
Title.....	Arsenas sodii seu Sodii arsenas;	Sodii arsenas.....	Arsenias sodicus.....	Arsenas natricus; sodii arsenas.	
	Arsenicicum natrium seu Natrium arsenicum.				
Requirement.....	The crystallized salt containing 36.85 per cent of arsenic acid.	Should contain in an uneffloresced condition not less than 98 per cent of di-sodium-ortho-arsenate.	Same as P. I.	Same as P. I.	
Liquor potassii arsenitis:					
Title.....	Arsenicalis liquor Fowleri seu Li-quorarsenicalis Fowleri seu Kali quorarsenicos liquor.	Liquor potassii arsenitis.....	Solutum arsenitis potassici.....	Liquor arsenicalis Fowleri.	
Requirement.....	Strength in arsenious acid, 1 per cent.	Should contain potassium arsenite corresponding in amount to 1 per cent of arsenic trioxide.	Same as P. I.	Same as P. I.	
Syrupus ferri iodidi:					
Title.....	Ferri iodidi sirupus seu Sirupus iodoti ferrosi seu Sirupus ferri iodati.	Syrupus ferri iodidi.....	Syrupus ioduri ferrosi; syrupus protioduri ferri.	Sirupus iodeti ferrosi.	
Requirement.....	Strength in anhydrous ferrous iodide 5 per cent.	About 5 per cent by weight of ferrous iodide; preserved with hy-pophosphorous acid.	Same as P. I.	Same as P. I.	
Tinctura cantharidis:					
Title.....	Cantharidis tinctura seu Tinctura Cantharidis.	Tinctura cantharidis.....	Tinctura alcoholica cantharidum.....	Tinctura cantharidum; cantharidis tinctura.	
Strength.....	10 per cent.....	10 gm. : 100 cc.....	10 per cent, with 1.5 per cent of cochineal.	Same as P. I.	
Menstruum:					
Requirement.....	Alcohol (70 per cent).....	Alcohol.....	Same as P. I.	Same as P. I.	
Tinctura iodi:					
Title.....	Iodi tinctura seu Tinctura iodi.....	Tinctura iodi.....	Not official.....	Solutio iodi spirituosae; tinctura iodi; iodi tinctura.	

2. COMPARATIVE TABLE SHOWING THE DEGREE OF COMPLIANCE, IN THE SEVERAL PHARMACOPŒIAS PUBLISHED IN 1905, WITH THE PROVISIONS OF THE BRUSSELS CONFERENCE—Continued.

	Protocol, International.	U. S. P., VIII.	Ph. Hisp., VII.	Ph. Ndl., IV.
Tinctura iodi —Continued.				
Strength.....	10 per cent.....	Iodine 7, potassium iodide 5 gm.; 100 cc.	Same as P. I.
Menstruum.....	Alcohol (95 per cent).....	Alcohol.....	Same as P. I.
Requirement.....	Color; physical properties.
Tinctura lobeliae :				
Title.....	Lobeliae tinctura seu Tinctura Lobeliae.....	Tinctura lobeliae.....	Tinctura alcoholica lobeliae.....	Tinctura lobeliae; lobelia tinctura.
Strength.....	10 per cent.....	10 gm.; 100 cc.....	Same as P. I.....	Same as P. I.
Menstruum.....	Alcohol (70 per cent).....	Diluted alcohol.....	Same as P. I.....	Same as P. I.
Requirement.....	Color; taste; sp. gr.; extract; qualitative tests.
Cocaine hydrochloridum :				
Title.....	Cocainum hydrochloricum.....	Cocaine hydrochloridum.....	Chlorurum cocainae; chlorhydras cocainae.....	Hydrochloras cocaini.
Requirement.....	The anhydrous salt.....	Same as P. I.; melting about 189.9° C.	Melting point 201° C.....	Melting point 183° C.
Unguentum hydragryi :				
Title.....	Hydragryi unguentum seu Unguentum Hydragryi.....	Unguentum hydragryi.....	Ponatum mercuriale; unguentum hydragryi.....	Unguentum hydragryi; unguentum neapolitanum.
Strength.....	30 per cent.....	50 per cent (unguentum hydragryi dilutum U. S. P. contains about 33 per cent Hg.)	Same as P. I. (ponatum mercuriale simplex, unguentum hydragryi simplex Ph. Hisp., contains 50 per cent Hg.)	Same as P. I. (unguentum hydragryi fortius Ph. Ndl. contains 50 per cent of Hg.)
Vinum antimoni :				
Title.....	Antimoniale vinum seu Vinum antimoniale; Stibiatum vinum seu Vinum stibiatum.	Vinum antimoni.....	Vinum emeticum; vinum antimoniale seu stibiatum.	Vinum stibiatum; stibiatum vinum; vinum emeticum.
Strength.....	In tartar emetic, 0.40 per cent.	Same as P. I.....	Same as P. I.....	Same as P. I.
Requirement.....	Color and physical properties.

3. DROPS.

The Ph. Ndl., IV, includes a table enumerating the number of drops required to weigh 1 gramme, of a number of official liquids. This table is based on the proposed standard drop measure.

The Ph. Hisp., VII, contains a table enumerating some 40 articles and pharmaceutical preparations and the number of drops required to weigh 1 gramme. The determinations were made at 15° C., with the international drop measure.

4. COMMENTS ON THE U. S. P., VIII, RELATIVE TO THE REQUIREMENTS OF THE BRUSSELS CONFERENCE FOR THE UNIFICATION OF THE PHARMACOPŒIAL FORMULAS FOR POTENT DRUGS.

An editorial, in commenting on the changes that have been made in the U. S. P., VIII, says:

An universal pharmacopœia has been a sort of Utopian dream for years, but it is eminently practicable for the pharmacopœia makers of different countries to "get together" on certain basic principles. Although we realize the annoyance and positive danger that lies in the changes just noted we can but feel a satisfaction that we are the first nation to issue a new pharmacopœia in which is embodied, as a result of the international conference, some of the recommendations proposed.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 263.

Williams, S. W., in commenting on these changes, says:

By adopting in part the recommendations of the international conference for the unification of formulas of potent medicaments, the committee of revision has taken a long step toward bringing about international uniformity in preparations of potent drugs.—*Ibid.*, p. 307.

Wilbert, M. I., points out that by comparing the formulas for preparations of potent drugs with the provisions of the protocol signed by the accredited representatives of civilized nations, at Brussels, in 1902, it will be found that our U. S. P. preparations still differ in many particulars from the proposed international standard.—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 361.

2. FOREIGN PHARMACOPŒIAS.

1. NETHERLANDS PHARMACOPŒIA.

The official title of the Netherlands Pharmacopœia is: *Pharmacopœa Nederlandica, Editio Quarta. Amstelodami, 1905*. It is printed in the vernacular and in Latin.

The Netherlands Pharmacopœia contains a total of 670 titles, including—

General formulas	17
Animal drugs.....	16
Vegetable drugs.....	184
Chemicals.....	182
Preparations	274

Among the new remedies admitted are the following titles: Acetanilidum, antipyrinum, sulfonalum, methylsulfonalum, phenacetinum, metadioxybenzolum (resorcin), salicylas antipyrini, saccharinum.

This pharmacopœia also includes monographs for Aether ad narcosin and Chloroformum ad narcosin.

Among the synonyms enumerated under the several official titles are antifebrinum, diureticum, lysolum, salolum, lanolinum, dermatolum, salipyrinum, formalinum, tannalbinum.

A drop table, based on the international standard dropper, is included. The weight of 20 drops of distilled water is given as being 1 gramme, while it requires 65 drops of ethyl acetate and 60 drops of alcohol to make the same weight.

The Netherlands Pharmacopœia contains a general heading for powders, and under this includes some general directions for the preparing of powdered drugs and the fineness of the several substances best suited for use (p. 307).

This pharmacopœia also includes, with the description of each preparation, a suggestion as to the color and the comparative density. It also contains suggestions on the odor and taste of the finished preparation and frequently specifies the specific gravity of liquid preparations and the amount of extractive that they should contain. With potent or alkaloidal drugs, assay processes are given, usually accompanied by qualitative tests.

The pharmacopœia also contains directions for first aid and a list of antidotes to be used in cases of poisoning (pp. 484-488).

No less than 19 pages are devoted to an enumeration of the substances to be used for the tests and the testing solutions of the pharmacopœia (pp. 489-507).

The Netherlands Pharmacopœia includes a table giving the specific gravity of a number of the more widely used articles at temperatures ranging from 12° to 35° C. This table includes ethyl acetate, acetic acid, the several mineral acids, ether, alcohol of different strengths, chloroform, bromoform, and ammonia (pp. 516-517).

2. SPANISH PHARMACOPŒIA.

The official title of the Spanish Pharmacopœia is: "Farmacopea Oficial Española, Séptima Edición." Madrid, 1905. It is printed in Spanish. The Pharmacopœia is the property of the Royal Academy of Medicine, and is revised by seven members of the Royal Academy of Medicine acting as a permanent revision commission.

Nineteen pages of the book are devoted to tables, including weights and measures, specific gravities, alcohol percentages, weight of drops, density of acids, and atomic weights; 9 pages are devoted to reagents and test solutions; 601 pages are devoted to monographs, descriptions,

and formulas; 66 pages are devoted to the indexes, one in Spanish and the other in Latin.

The total number of pages indexed is 698, and the book contains a total of 1,073 titles, including:

Animal drugs	26
Vegetable drugs	243
Chemicals	260
Preparations	544

A review (in the *Brit. & Col. Druggist*, Lond., 1905, v. 48, p. 240) points out that among the several modifications that have been adopted are:

1. The exclusive use of the metric system of weights and measures, the alternate apothecaries weights of the 1884 edition being discarded.
2. The inscription of quantities in letters as well as figures.
3. The strict adherence to the simple alphabetical arrangement.
4. The official acceptance of the decisions of the Brussels Conference.

The arrangement is alphabetical, according to the Spanish titles, the Latin titles being given secondarily.

Among the newer remedies included in the Spanish Pharmacopœia are the following Latin titles:

Anthipirina, aristolum, bioxidum natri, cantharina, euchinina, exalgina, formol, ichthyol, salicylas phenolicus, sulphonalum, theobromina, trionalis, urethanum, xeroformicum, iodol.

The Spanish Pharmacopœia differentiates between *extracto acuoso*, *extracto alcoholico*, and *extracto fluido*.

This pharmacopœia also includes suggestions for the medicinal uses of the several articles.

Three formulas for ophthalmic discs or lamellæ are included; these are for lamellæ of atropine sulphate, cocaine hydrochloride, and eserine salicylate, using a gelatin base.

The pharmacopœia contains two formulas for artificial serum (*Serum artificiale ex Hayem*); the first formula calls for—

	Parts.
Pure sodium chloride	5
Pure sodium sulphate, in crystals	10
Sterilized distilled water	1,000

The second formula:

	Parts.
Pure sodium chloride	8
Sterilized distilled water	1,000

The salts are to be dissolved in the sterile distilled water, the resulting liquid filtered, and again sterilized.

The Spanish Pharmacopœia contains a description and a method for the assay of diastase.

Under the title "Digitalina" the Spanish Pharmacopœia includes a description of crystallized digitalin and amorphous digitalin. The dose of the crystallized variety is given as being 0.25 milligrammes and of the amorphous variety as 1.00 milligramme.

Under the title "Ergotina" the Spanish Pharmacopœia includes a formula for making an aqueous extract of ergot.

The pharmacopœia also includes descriptions and tests for, with methods of making, glycerophosphate of calcium and glycerophosphate of sodium.

Under the Latin title "Essentia citræ" the Spanish Pharmacopœia describes an essential oil obtained by expression or by distillation, with the intervention of water, from the epicarp of the citron.

Under the Latin title "Peptona" the Spanish Pharmacopœia gives directions for making and describes the properties of a beef peptone.

3. BRITISH PHARMACOPŒIA.

MacAllister, Donald, in his presidential address to the general medical council, at the meeting held on May 23, 1905, in referring to the coming revision of the British Pharmacopœia, said:

The pharmacopœia committee has decided that it is expedient to appoint committees of reference to advise it on points of chemistry, botany, pharmacology, and pharmacy. With the courteous assistance of the pharmaceutical societies of Great Britain and Ireland a committee of reference in pharmacy has first been appointed. It consists of expert pharmacists, with Mr. Hills as chairman and Professor Greenish as secretary, to whom questions relating to pharmacopœial pharmacy will be referred for investigation and report.—Quoted in *Am. J. Pharm., Phila.*, 1905, v. 77, p. 441.

A committee appointed by the Council of the Pharmaceutical Society of South Australia, submits suggestions as to specific preparations and a list to be made official, to be included in the Indian and Colonial Addendum to the British Pharmacopœia. It was also recommended that the pharmacopœia be published in double form, a small manual for the physician, omitting characters, tests, and appendices; and a complete text-book for the pharmacist.—*Pharm. J. Lond.*, 1905, v. 21, p. 679.

For some editorial comments on pharmacopœial revision see *Ibid.*, p. 684.

4. ITALIAN PHARMACOPŒIA.

van Schoor, Oscar, reviews the new Italian Pharmacopœia, including detailed enumerations of the tests and descriptions.—*J. Pharm. d'Anvers*, 1905, v. 61, pp. 1-15 and 41-57.

A review of a reprint of the above articles.—*Bull. Soc. roy. de Pharm. Bruxelles*, 1905, v. 49, p. 148.

5. DANISH PHARMACOPŒIA.

Crunsberg, A., discusses a number of articles proposed for admission to the new Danish Pharmacopœia.—Arch. f. Pharm. og Chem. Copenhagen, 1905, v. 12, p. 156.

6. SWISS PHARMACOPŒIA.

Wilbert, M. I., points out that the commission having the revision of the present Swiss Pharmacopœia in charge has made it a practice to publish, from time to time, bulletins announcing the progress that is being made and the more important changes that are proposed or accepted. One of the more recent of these bulletins (Schweiz. Wehnschr. f. Chem. u. Pharm. 1905, p. 531) announces the proposed changes in connection with a number of galenical preparations.—Am. J. Pharm., Phila., 1905, v. 77, p. 584:

SPANISH EDITION OF THE U. S. P.

An editorial in the American Druggist (1905, v. 47, p. 230) suggests the publication of a Spanish edition by the trustees of the U. S. P.

A later editorial comments favorably on the decision of the trustees of the United States Pharmacopœial Convention to translate the United States Pharmacopœia into Spanish.—*Ibid.*, p. 343.

Ebert, A. E., in commenting on the decision of the U. S. P. trustees, to publish a Spanish edition, says:

All that will be necessary will be to translate the work from one language into another, and it is believed that this can be accomplished and that the volume can appear in the new tongue within a year.—*Ibid.*, p. 358.

An editorial comments favorably on the decision to publish a Spanish edition of the U. S. P.—Western Druggist, Chicago, 1905, v. 27, p. 764.

Wilbert, M. I., discusses the desirability of a Spanish edition of the U. S. P., the various suggestions that have been made regarding it, and calls attention to resolutions adopted at the meeting of the International Sanitary Conference of the Pan-American Republics held in Washington, October 10-14. 1905.—Am. J. Pharm., Phila., 1905, v. 77, p. 583.

The resolutions referred to above are, in part, as follows:

Whereas this revised pharmacopœia embraces many new forms of value both for use in therapeutics and prevention of epidemic disease, and represents the best thought and labor of experts on these matters: Therefore, be it

Resolved, That a translation of this United States Pharmacopœia into the Spanish language would prove of great benefit to the medical profession and pharmacists in each of the republics represented in this convention; and further

Resolved, That the said pharmacopœia be referred to the several Governments to report upon at the next meeting in Mexico, with a view to the adoption of an international pharmacopœia for the American Republics.—See also J. Am. M. Ass., 1905, v. 45, p. 1348.

PHARMACOPŒIAL HISTORY.

Tschirch, A., in a review of some of the older pharmacopœias makes the point that these books accurately reflect the medical and pharmaceutical practices of their time and are thus doubly interesting from a historic point of view.—Reprinted in Pharm. Post. Wien, 1905, v. 38, p. 389, ff. from Schweiz. Wehnschr. f. Chem. u. Pharm.

III. COMMENTS ON OFFICIAL ARTICLES.

ACACIA.

Smith, R. Grieg, reports some experiments with the microorganisms which produce the gums of the arabin group and believes that he is able to demonstrate that the gums of the cerasin group are produced by the same organism. (From Proc. Linn. Soc. N. S. Wales, 1904, p. 217.)—Biochem. Centralbl., 1905, v. 4, p. 436.

Goris and Lefèvre (Pharm. Zentralh. v. 46, p. 491) recommend, as a substitute for acacia, the gum from *Analgeissus latifolia* and *A. pendula*, both found in India.—Merck's Rep., N. Y., 1905, v. 14, p. 281.

An abstract (from Ph. Zeit.) points out that the detection of acacia in tragacanth is based on the presence of oxydase in acacia and its absence in tragacanth. A solution of acacia (1-30) in cold water, is shaken out with equal parts of 1 per cent guaiacol and 1 drop of H_2O_2 solution. The mixture turns rapidly brown when acacia is present, remaining colorless with pure tragacanth.—Apothecary, Boston, 1905, v. 17, p. 540.

An abstract calls attention to a recent study of the subject by Bourquelot (quoted in Pharm. Zentralh. Aug. 10, 1905) in which he calls attention to the possibility of acacia, because of its oxidizing properties, being the cause of decomposition in mixtures. A number of practical illustrations and experiments are recorded.—Am. Druggist, N. Y., 1905, v. 47, p. 239.

An abstract (from Suedd. Apoth. Ztg.) enumerates a number of substances that are incompatible with acacia, among them phenol, thymol, pyrogallol, guaiacol, creosol, vanillin, morphine, apomorphine, eserine, adrenalin, preparations containing tannin, coal-tar preparations, and substances readily decomposed by oxidation.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 30.

Weiss recommends the dilution of opium with acacia.—Pharm. Zentralh., 1905, v. 46, p. 65.

Weigel objects to this, and asserts that the extract prepared from such an opium, rich in gum, would certainly be low in morphine percentage. (*Ibid.*, p. 189.)—Am. Druggist, 1905, v. 47, p. 239.

Firbas, Richard, reviews the literature and concludes that in solutions containing mucilage of acacia morphine is slowly decomposed into oxymorphine.—Pharm. Post, Wien, 1905, v. 38, p. 735.

Beal, J. H., in discussing the new pharmacopœia says:

The use of 33 per cent of lime water in the formula for mucilage of acacia is an improvement, in that it corrects the common acid condition of old gum and aids in its keeping qualities.—*Midland Druggist*, 1905, v. 6, p. 1035.

Pinchbeck, G. (*Pharm. J.*, Lond., v. 20, p. 620), suggests that mucilage of acacia should be officially directed to be heated to 100° C. to eliminate the oxidase. Tabulated results of some experiments made are included.—*Year Book Pharm.*, Lond., 1905, p. 225.

White, Edmund, records some experiments that were undertaken to determine the comparative viscosity of the simple and mixed mucilages.—*Pharm. J.* Lond., 1905, v. 21, p. 133.

Devalmont (*Oesterr. Zeitschr. f. Pharm.*, 1905) asserts that because of the contained oxydase, acacia is incompatible with eserine, adrenalin, and morphine. Continued heating to 100° C. destroys this ferment and the resulting substance is no longer incompatible with the above alkaloids.—*Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 142.

Just's *Botanischer Jahresbericht* (for 1905, v. 33, part 3, p. 786) contains a number of additional references on gums of the acacia type.

ACETANILIDUM.

Herting, Otto, outlines a method for determining the melting point of this substance.—*Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 72.

Riedel's *Berichte* compares the requirements of the Ph. Germ., IV, with the findings of independent investigators. After some additional experimentation, on the part of the chemists in Riedel's laboratory, it was decided that the figures given by Beilstein are more nearly correct, and that at a barometric pressure of 760 mm. the boiling point of acetanilide is 302.45° C., or about 7.45° C. higher than the boiling point required by either the Ph. Germ., IV, or the U. S. P., VIII.—*Riedel's Berichte*, Berlin, 1905, p. 40.

Raikow and Külümow point out that acetanilide does not react with Nessler's solution at ordinary temperatures, and even on heating only a partial production of unstable mercuric iodide results.—*Oesterr. Chem. Ztg.*, 1905, v. 8, p. 448.

Rosenthaler, L., points out that with Millon's reagent acetanilide gives a yellowish green color that gradually changes to orange, and finally to dark brownish red. In contradistinction to phenacetin, the liquid remains clear. (See also acetphenetidin.)—*Abstract* (from *Suedd. Apoth. Ztg.*) *Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 86.

Fulmer (*Ann. d. Chim. Analyt.*, 1905) suggests the following test for acetanilide in phenacetin:

One decigramme of the suspected substance is boiled for one minute with 1 cc. of concentrated hydrochloric acid; the mixture is then diluted with 10 cc. of water and filtered. To the filtrate are added three drops of a 3 per cent solu-

tion of chromic acid. If the phenacetin is pure the solution assumes a ruby red color, which is permanent. If it contains acetanilide the solution assumes a dark green tint, and later a deposit is observed.—*Abstr. Am. Druggist, N. Y., 1905, v. 47, p. 320.*

Puckner, W. A., discusses the estimation of acetanilide and records a number of experiments that were made under varying conditions.—*Proc. Am. Pharm. Ass., 1905, v. 53, pp. 289-292.*

Puckner, W. A., discusses the estimation of acetanilide in presence of caffeine; points out some of the difficulties that have been encountered and records a number of experiments.—*Ibid., pp. 292-298.*

A report of a subcommittee of the council on pharmacy and chemistry of the American Medical Association gives the percentage proportion of acetanilide, caffeine, and sodium bicarbonate in each of several of the more widely advertised acetanilide mixtures. Diluents and other constituents than those mentioned in the report were not determined. The substances reported on, and their percentage content of the substances mentioned, were (*J. Am. M. Ass., Chicago, 1905, v. 44, p. 1790*):

Ammonol.—Acetanilide, 50; sodium bicarbonate, 25; ammonium carbonate, 20.

Antikamnia.—Acetanilide, 68; caffeine, 5; citric acid, 5; sodium bicarbonate, 20.

Phenalgin.—Acetanilide, 57; sodium bicarbonate, 29; ammonium carbonate, 10.

Salacetin.—Acetanilide, 43; sodium bicarbonate, 21; sodium salicylate, 20.

Kohler's Headache Powder.—Acetanilide, 76; caffeine, 22.

Orangeine.—Acetanilide, 43; sodium bicarbonate, 18; caffeine, 10.

An unsigned article, under the caption "Acetanilide, A Slandered Drug," discusses the comparative pharmacologic action and the medicinal properties of acetanilide and phenacetin.—*The New Idea, 1905, v. 27, pp. 66-69.*

Stengel, Alfred, reports two additional cases of chronic acetanilide poisoning.—*J. Am. M. Ass., Chicago, 1905, v. 45, pp. 243-245.*

Probasco, E. B., discourses on acetanilide poisoning.—*N. Y. State J. Med., 1905, v. 5, pp. 318-320; also in Deut. Med. Presse, Berlin, 1905, v. 9, pp. 135. Reference from Ind. Med., 1905, p. 1052.*

ACETONUM.

Hinrichs, Carl G., says:

From old Roger Bacon till to-day is a long cry; his spirit has just been made official. Acetone is an excellent solvent for organic as well as inorganic compounds, especially mercuric salts. It is a good addition to the U. S. P.—*Am. J. Pharm., Phila., 1905, v. 77, p. 506.*

Francis, John M., points out that the specification of 99 per cent pure acetone demands a grade not easily procurable, and furthermore such purity is not guaranteed by the other specifications and tests

appended. Occasional lots of commercial acetone have a "specific gravity of 0.790 at 25° C. and begin to boil at 56.5° C.;" but our experience has been that practically all yield from 20 to 45 per cent distilling above 56.5° C. Perhaps the distillers will produce an exceptionally pure acetone for pharmacists' use, but we doubt if it will be generally procurable for a long time.—Bull. Pharm., Detroit, 1905, v. 19, p. 317.

Herting, Otto, discusses some of the characteristics of acetone, its uses and the tests for purity and identity, also some suggestions as to its production.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 72.

Pastureau presents a study of the action of hydrogen peroxide on acetone.—J. de pharm. et de chim., Paris., 1905, v. 22, p. 14.

An abstract discusses the determination of acetone, by the iodoform method, as presented by various authors.—Abstr. J. Soc. Chem. Ind. Lond., 1905, v. 24, p. 460.

Ziegler, J., discusses the official (German) test for acetone and believes it to be not alone practical, but also readily applied.—Apoth. Ztg., Berlin, 1905, v. 20, p. 822.

Barth, Franz, discusses the difficulties that are met in testing spirit of mustard, of the Ph. Germ., IV, for acetone.—*Ibid.*, p. 758.

Laserre, A., publishes a preliminary report of a study of the action of aldehydes and of acetone on solutions of mercuric acetate.—J. de pharm. et de chim., Paris, 1905, v. 22, p. 241.

Frommer, Victor (Berl. Klin. Wchnschr., 1905, p. 1008), outlines a method for the detection of acetone in urine. To about 10 cc. of urine add 1 gm. of potassium hydrate and without waiting for the latter to dissolve add 10 to 12 drops of salicylaldehyde; heat the mixture to about 70° C. and allow to stand. The presence of acetone is indicated by a deep purplish zone at the juncture of the two fluids.—Apoth. Ztg., Berlin, 1905, v. 20, p. 629.

ACETPHENETIDINUM.

Herting, Otto, discusses the nomenclature, some of the chemical characteristics, and the tests for acetphenetidin.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 85.

An editorial, in discussing the additions to the U. S. P., VIII, says, under acetphenetidin:

No inkling is given either under this head or under the other synthetics introduced that these preparations are known popularly under other names, and while in some cases the chemical description has been shortened there has been no attempt to introduce substitutes for the trade names.—Drug Topics, 1905, v. 20, p. 195.

Rosenthaler, L. (from Suedd. Apoth. Ztg.), points out that with Millon's reagent phenacetin gives an intense violet color that changes

to a brown red and finally to a light brown. In the solution are formed light yellow crystals of nitrophenacetin. (See, also, acetanilide.)—Deut.-Amer. Apoth. Ztg., 1905, v. 26, p. 87.

Maurice, J. (Ann. de la soc. de méd. de Gand., 1905, p. 158), reports the case of a woman who was poisoned by the ingestion of 11 grammes of phenacetin.—Biochem. Centralbl., 1905, v. 4, p. 547.

Hirschfeld, Max (Deut. Med. Wchnschr., 1905, No. 2), reports a case of chronic phenacetin poisoning, manifested by small punctate abscesses above the ankles.—Pharm. Zentralh. 1905, v. 46, p. 727.

ACIDUM ACETICUM.

Herting, Otto, discusses the production and the uses of acetic acid, and compares the U. S. P., VIII, and Ph. Germ., IV., tests and requirements.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 86.

Riedel's Berichte discusses the boiling point of acetic acid of the Ph. Germ., IV, and agrees with the statement made by the Chemiker Kalender that the higher limitation for the boiling point of acetic acid is too low and should be raised to 119° or 119.5° C.—Riedel's Berichte, Berlin, 1905, p. 41.

Rossi (L'Industria chimica, v. 6, p. 253) determined the amount of sulphuric acid in commercial acetic acid by making use of the fact that the latter is indifferent to methyl orange in alcoholic, formaldehyde, or, especially, acetone solution, so that the sulphuric acid may be titrated with sodium hydroxide in any one of these solutions.—Abstr. J. Am. Chem. Soc., N. Y., 1905, v. 27, p. 1346.

Kebler, Lyman F., reports the finding of acetic acid containing chloride, sulphate, and lead.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 182.

Kebler, Lyman F., in a report on the testing of chemical reagents, comments on the lack of precaution shown in the marketing of glacial acetic acid, as well as some other products used as reagents.—Proc. Ass. Off. Agr. Chem., 22 Ann. Conv. (1905), p. 185.

ACIDUM BENZOICUM.

Bigelow, W. D., in a report on preservatives, points out the difficulty that has been met with in the detection of benzoic acid. The subject has been studied by Charles S. Ash, who reports his results.—Proc. Ass. Off. Agr. Chem., 22 Ann. Conv. (1905), p. 86.

Moerk, F. X., in discussing the detection of benzoic and salicylic acids, refers to the formation of more or less permanent emulsions, for the avoidance of which he recommends saturating the liquid with salt and extracting the resulting solution with chloroform.—Am. Druggist, N. Y., 1905, v. 47, p. 38.

Lloyd, John Uri, points out that—

The Eclectic School of Medicine employs only the natural benzoic acid, made from gum benzoin, and rejects that urine made regardless of reaction. In the commercial world very little of this natural acid is distributed, owing to its expense. It can be safely said that if one wishes benzoic acid made from gum benzoin instead of urine he will necessarily be forced to give the subject his personal attention. The same is true of the benzoates made therefrom, including both common and rare in medicine.

The editor adds:

Attention should be directed to the fact that most of the commercial benzoic acid of to-day is made from toluene.—Pharm. Rev., 1905, v. 28, p. 298.

Douglass, Malcolm E., in notes on materia medica, suggests its use in concretions in the joints, affections of the bladder, nocturnal enuresis, and in rheumatism.—Hahneman. Month., Phila., 1905, v. 40, p. 604.

ACIDUM BORICUM.

Herting, Otto, discusses the tests for identity and purity and compares the requirements of the Ph. Brit., IV, and Ph. Germ., IV.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 142.

Kebler, Lyman F., reports finding "boric acid C. P." which contained phosphate and a trace of magnesium.

Patch found one lot of boric acid which contained calcium and sulphate.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 182.

An unsigned article points out that boric acid frequently gives evidence of containing chlorides.—Suedd. Apoth. Ztg., 1905, v. 45, p. 758.

Windisch, Karl, reviews several of the methods proposed for the estimation of boric acid, the difficulties met, and the various attempts made to overcome them.—Ztschr. f. Unters. d. Nahr. u. Genussm., Berlin, 1905, v. 9, p. 641.

v. Spindler, O., reviews some of the recent literature bearing on the demonstration of boric acid and describes and figures a new apparatus designed to facilitate the application of the methyl alcohol hydrogen flame test for boric acid.—*Ibid.*, 1905, v. 10, p. 478.

v. Spindler, O., records a number of experiments and outlines a method for determining the amount of boric acid, either free or in combination.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 445.

Fendler, G. (Apoth. Ztg., v. 20, p. 757), discusses the turmeric reaction for boric acid and outlines a method recommended as giving an admirable test paper in so short a time that it is not necessary to keep a stock.—Abstr. Pharm. J., Lond., 1905, v. 21, p. 617.

Goske, A., points out that the generally used turmeric paper test for boric acid and boric acid compounds is not free from possible objections in that it is too delicate, table salt that is not entirely free

from boron giving a distinct reaction.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, Berlin, 1905, v. 10, p. 242.

Fendler, G., reviews the literature and the tests bearing on the detection of boric acid when used as a preservative in foodstuffs.—*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 757.

Hefelmann, Rudolf, discusses the demand that has been made to provide for the quantitative estimation of boric acid in all cases where it occurs in foods preserved with salt. The author concludes that the amount of boric acid in salt is so minute that it would not likely be found as such in the course of the ordinary inspection analysis.—*Ztschr. f. öffentl. Chem.* 1905, v. 11, pp. 231–234.

Vaubel and Bartelt (*Chem. Zeit.*, 1905, v. 29, pp. 630–631), point out that sulphurous acid in solution in which boric acid is to be determined by titration in the presence of glycerol, using phenolphthalein as an indicator, must be removed by a preliminary treatment, otherwise too low results are obtained. To accomplish this they recommend boiling the solution after the addition of a strong mineral acid.—*Analyst*, London, 1905, v. 30, p. 285.

An abstract (from *Chem. Ztg.*, 1905, No. 46) reviews the several tests devised for the quantitative estimation of boric acid.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 563.

Windisch, K. (*Ztschr. f. Unters. d. Nahr. u. Genuss.*, v. 9, p. 641), outlines a method for the determination of boric acid in wines, fruit-juices, etc.—*Pharm. J.*, Lond., 1905, v. 21, p. 230.

Rost, E. (*Deutsch. Med. Wochnschr.*, No. 2, 1905), discusses the effect of boric acid and borax on the animal organism, controverting the statements made by Liebreich.—*Nouv. Rem.*, 1905, v. 21, p. 452.

Rost, E. (*Arch. internat. de Pharmacod.*, 1905, v. 15, p. 291), reports a number of observations on rabbits, dogs, and men, bearing on the absorption and elimination of boric acid. A comprehensive literature of the subject, comprising practically all that has been published regarding pharmacologic, bacteriologic, therapeutic, and toxicologic properties of boric acid is appended.—*Biochem. Centralbl.* 1905, v. 4, p. 447.

Abstract (from *La Nuova Riv. Terap.*, No. 1, 1905) includes a report of five fatal cases of poisoning by boric acid, to which Frank H. Pritchard adds a case of alarming prostration from intestinal irrigations, but with recovery.—*Hahneman. Month.*, Phila., 1905, v. 40, p. 386.

ACIDUM CAMPHORICUM.

An editorial, in discussing the additions to the U. S. P., VIII, says of camphoric acid:

Presumably introduced out of deference to German opinion, as it is not very extensively used here.—*Drug Topics*, 1905, v. 20, p. 195.

Herting, Otto, discusses the production of camphoric acid and its structural formula.—*Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 99.

ACIDUM CITRICUM.

Herting, Otto, discusses the composition of citric acid, its production at the present time, and the possibility of its production by biologic processes.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 100.

Heingartner, A. (*Consular Rpts.*, U. S., 1905), describes a method of extracting citric acid from lemon waste direct, which is reported to have been discovered by Giovanni Restuccia, of Italy.—*Exp. Sta. Rec.*, v. 17, No. 4, p. 401.

Kebler, Lyman F., reports finding citric acid containing lead.

Patch found one lot containing lead and iron, while ten lots, containing traces of iron and of sulphur, averaged 99.5 per cent pure.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

In an unsigned article it is pointed out that citric acid has been found to contain heavy metals and sulphates, probably due to sophistication of the technical product.—*Suedd. Apoth. Ztg.*, 1905, v. 45, p. 758.

Williams, John K., suggests a formula for syrup of citric acid in which he proposes the use of extract of lemon (from the oil and from the fresh peel) instead of the tincture, with the addition of glycerin.—*Proc. Connecticut Pharm. Ass.*, 1905, p. 49.

ACIDUM GALLICUM.

Herting, Otto, discusses some of the reactions of gallic acid and of tannin, their relations, and their several uses.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 100.

ACIDUM HYDROBROMICUM DILUTUM.

Herting, Otto, discusses the production of hydrobromic acid, the impurities found in it, and suggests a method for preparing hydrobromic acid from bromine and methyl alcohol.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 141.

ACIDUM HYDROCHLORICUM.

Herting, Otto, discusses the composition of hydrochloric acid, its manufacture, and the production of a chemically pure article.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 128.

Staedel, W. (*Chem. Ind.*, 1905, v. 28, pp. 173-178, 198-204, 226-232), presents a study of the Hargreaves process for the manufacture of hydrochloric acid and records a number of laboratory experiments designed to elucidate the nature of the reactions occurring in this process.—*Abstr. J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 439-440.

An abstract (from *Apoth. Ztg.*, 1905, v. 20, p. 932) discusses the purification of hydrochloric acid by treatment with strong solution of vanadous chloride.—*Abstr. Pharm. J., Lond.*, 1905, v. 21, p. 910.

Kebler, Lyman F., found hydrochloric acid containing free chlorine.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

Burke, W. J., examined 25 samples of diluted hydrochloric acid; 2 were practically of the U. S. P. strength, 10 below, and 13 above: ranging from 8.5 to 13.3 per cent.—*Proc. Massachusetts Pharm. Ass.*, 1905, p. 106.

Ferguson, W. C., publishes a table of specific gravities of hydrochloric acid varying in composition from 5.73 to 42.57 per cent of HCl.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 786.

Küster and Muench publish a table designed to facilitate the preparation of normal hydrochloric acid solutions, based on the specific gravity of the acid used.—*Ber. d. deutsch. chem. Gesellsch.*, 1905, v. 38, pp. 150–152.

Neumann, A. (*Pharm. C. H.*, 1905, No. 40), figures and describes an apparatus designed for the demonstration and the estimation of hydrochloric acid in stomach content, particularly when the latter is available in but small quantities.—*Pharm. Ztg., Berlin*, 1905, v. 50, p. 927.

ACIDUM HYDROCYANICUM DILUTUM.

Herting, Otto, discusses some of the tests given in the U. S. P., VIII, and recommends hydrogen peroxide as an efficient antidote in case of poisoning.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 142.

Guerin, M. G., discusses the methods proposed by Liebig and by Fordos and Gélis for the titrimetric estimation of hydrocyanic acid, and proposes a modification which consists essentially in the addition of a solution of sodium borate to the hydrocyanic acid containing liquids before titrating with silver nitrate.—*J. de pharm. et de chim.*, Paris, 1905, v. 22, p. 433.

Weehuizijn, F., discusses phenolphthalin as a reagent for hydrocyanic acid (*Pharm. Weekblad*, 1905, v. 42, pp. 271–272):

If an alkaline solution of phenolphthalin, together with a 1:2000 solution of copper sulphate be added to a solution of hydrocyanic acid a red coloration is produced in the cold, the phenolphthalin being oxidized to phenolphthalein. A perceptible coloration is produced in a solution containing 1:500000 hydrocyanic acid.—*Abstr. J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 562.

McDowall (*Chem. News*, v. 89, p. 229) outlines a method for the determination of hydrocyanic acid in cyanides by the use of an ammoniacal solution of copper sulphate. The disappearance of color is sharp and the presence of chlorine is without influence.—*Abstr. J. Am. Chem. Soc.*, 1905, v. 27, p. 1340.

Umney and Bennett, in discussing the essential oils of the U. S. P., VIII, say:

There is at the outset a difficulty in preparing magnesium hydroxide free from chlorine * * *. The process appears to yield lower results than those we have obtained on a manufacturing scale in the removal of hydrocyanic acid from bitter-almond oil, but we have not, so far, had the opportunity of comparing the various processes. Our records, extending over a great many years, would appear to indicate in the freshly prepared oil of bitter almond a higher proportion of hydrocyanic acid than 4 per cent.—Pharm. J., Lond., 1905, v. 21, p. 145.

Guignard, L., discourses on the presence of a compound furnishing hydrocyanic acid in the leaves of *Sambucus nigra*.—Compt., rend. Acad. d. sc., Paris, 1905, v. 141, pp. 16–20, 236–238, 1193–1201.

Bourquelot and Danjou present a study of the glucoside in *Sambucus nigra* L., which produces hydrocyanic acid. They also discuss the method used to isolate the glucoside.—J. de pharm. et de chim., Paris, 1905, v. 22, pp. 154, 219, 385.

van Itallie, L., presents an elaboration of the work of Bourquelot and Danjou: he was able also to demonstrate the formation of hydrocyanic acid in the leaves of other plants.—*Ibid.*, p. 337.

Jouck, Karl, reports some experiments made to isolate the hydrocyanic-acid producing substances in cherry laurel leaves and in the bark of *Prunus padus*.—Arch. d. Pharm., 1905, v. 243, p. 421.

Burford, Madden, and Goldsbrough discuss the recovery, under hydrocyanic acid, from acute epileptic seizures occurring after abdominal section.—Hahneman. Month., Phila., 1905, v. 40, p. 395.

ACIDUM HYDRIODICUM DILUTUM.

Herting, Otto, discusses the production and the tests for purity of hydriodic acid.—Deut.-Amer. Apoth. Ztg., 1905, v. 26, p. 141.

ACIDUM LACTICUM.

Herting, Otto, discusses the several tests that have been included in the U. S. P., VIII, and suggests that they are rather excessively numerous for an article of such comparatively minor importance as lactic acid.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 100.

Croner and Cronheim (Biochem. Centralbl., 1905, v. 4, p. 357) suggest a new test for lactic acid based on its conversion into iodoform under the influence of iodine and an alkali, and the formation of isonitrile from the iodoform by the action of a primary amino base. Obviously alcohol and acetone, which react in the same way as lactic acid, must be eliminated from the liquid, by heating, before the test is applied.—Analyst, London, 1905, v. 30, p. 403.

White, Gordon, discusses the use of lactic acid in pyorrhea alveolaris.—Dental Cosmos, Phila., 1905, v. 47, p. 152.

Kirk, Edward C., recommends the use of lactic acid for the removal of tartar, for which it has advantages over sulphuric acid.—*Ibid.*, p. 753.

Chandler, Swithin, recommends the use of lactic acid as an injection in cases of acute as well as chronic gonorrhœa in the female.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 1071.

ACIDUM NITRICUM.

Herting, Otto, discusses the composition of nitric acid, the material from which it is made, and the average composition of this material.—Deut.-Amer. Apoth. Ztg., 1905, v. 26, p. 128.

Winteler, F., discusses the economic questions involved in the commercial production of nitric acid.—Chem. Ztg., Cöthen, 1905, v. 29, pp. 689, 820.

Guttmann, Oscar, makes some additional explanation in connection with the points raised by Winteler on the economic production of nitric acid.—*Ibid.*, p. 934.

Ferguson, W. C., gives a table of specific gravity of nitric acid varying in composition from 14.49 to 95.80 per cent of HNO_3 .—J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 785.

Lunge, G., controverts the criticism made by Winteler on the estimation of nitric acid by means of the specific gravity.—Chem. Ztg., Cöthen, 1905, v. 29, p. 933.

Stavenhagen, A., discusses the oxidation of nitrogen by means of the discharge of high tension electrical currents, reviews the subject, and records some experiments that were made.—Ber. d. deutsch. chem. Gesellsch., 1905, v. 39, pp. 2171–2177.

Witt, O. N., reviews the work in connection with the utilization of atmospheric nitrogen. Also an account of the practical application of the work, as carried out in Norway in the production of nitric acid and nitrates.—Apoth. Ztg., Berlin, 1905, v. 20, p. 1009.

Küster and Muench record some experiments made in the production of absolute nitric acid, in the form of snow white crystals, at a temperature below -41°C . These crystals melt to a yellowish liquid, containing nitrogen pentoxide and water.—Ztschr. f. anorgan. Chem., 1905, v. 43, pp. 350–355.

Rumpf, K., comments on the proposed use of colorless, fuming nitric acid in place of the official (German) fuming nitric acid and points out that the colorless acid will serve for many of the tests that are provided for the ordinary red acid, though it does have some characteristics that would appear to differentiate it from the latter.—Pharm. Ztg., Berlin, 1905, v. 50, p. 640.

Gutbier, A., reviews the available methods for determining nitric acid and nitrates and recounts some experiments made with

"nitron" as a readily available means for estimating the quantity as well as detecting the presence of nitric acid and nitrates.—Ztschr. f. angew. Chem., 1905, v. 18, pp. 494-499.

Busch, M., discusses the gravimetric estimation of nitric acid by means of "nitron," the diphenyl-endanilo-dihydro-triazole, the use and preparation of which is described. (Ber. 1905, v. 38, pp. 856-860.) Nitron is said to be efficient for the detection of nitric acid, free or combined; 1:60000 at ordinary temperature, 1:80000 at 0° C. Also for the determination of nitric acid and for the detection as well as the determination of nitrate in the presence of nitrites.—Abstr. J. Soc. Chem. Ind., Lond., v. 24, 1905, p. 292.

Pfyl, B., proposes a simple method for the estimation of nitric acid in the presence of organic substances. This consists in the reduction of the nitric acid to nitric oxide by means of ferrous chloride and hydrochloric acid, washing the gas with 15 per cent solution of sodium hydrate in the absence of air and passing the resulting washed gas into a 1/10 N. permanganate solution to absorb the nitric oxide. The excess of permanganate solution is then titrated back with ferrous oxide.—Ztschr. f. Unters. d. Nahr. u. Genussm., Berlin, 1905, v. 10, p. 101.

Meisenheimer and Heim discuss the determination of nitric acid and nitrous acid.—Biochem. Centralbl., 1905-6, v. 4, p. 567.

Frerichs, G., calls attention to the fact that diphenylamin is not always directly applicable for the demonstration of nitric acid in solutions, and advises the washing out of the nitric acid with ether and the use of this ethereal solution for the test with diphenylamin. As sulphuric acid reacts violently with ether, the diphenylamin solution should be added carefully drop by drop. (From Arch. d. Pharm., 1905.)—Abstr. Pharm. Zentralh., 1905, v. 46, p. 947.

Burke, W. J., examined 25 samples of dilute nitric acid; 2 were of the U. S. P. strength, 10 below, and 13 above; ranging from 7.5 to 17.9 per cent of HNO_3 .—Proc. Massachusetts Pharm. Ass., 1905, p. 105.

Hall and Cooper consider the effects of the inhalation of the fumes of nitric acid.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 396.

ACIDUM PHOSPHORICUM.

Herting, Otto, discusses the composition and tests for phosphoric acid.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 155.

Patch, Edgar L., found samples of phosphoric acid that contained traces of iron and of silica; one lot was mostly metaphosphoric acid.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 182.

Arnold and Werner (Chem. Ztg., 1905, v. 29, pp. 1326-1327) point out that the published reactions for phosphoric acid have been shown to be generally unreliable; they suggest a new series of tests

with the alkali salts of ortho-, pyro-, and meta-phosphoric acids.—*Exp. Sta. Rec.*, v. 17, No. 11, p. 1037.

Baxter and Griffin discuss the determination of phosphoric acid by means of ammonium molybdate. The conclusions arrived at include the assertion that it is possible to obtain ammonium phospho-molybdate constant in composition and in a state suitable for weighing, so that it may be used for the accurate estimation of phosphoric acid. The precipitate must be formed by pouring the phosphate into the molybdic acid. If the precipitation is performed in the reverse manner the composition of the precipitate varies considerably.—*Am. Chem. J.*, 1905, v. 34, pp. 204–217.

Hirt and Steel outline a rapid volumetric method for the determination of phosphoric acid.—*Chem. News, Lond.*, 1905, v. 92, pp. 113–114.

Raschig, F. (*Z. angew. Chem.*, 1905, v. 18, pp. 374–376), discusses the volumetric estimation of phosphoric acid.—*Abstr. J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 350.

ACIDUM SALICYLICUM.

Herting, Otto, presents some remarks on the history, composition, and uses of salicylic acid.—*Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 113.

Kebler, Lyman F., reports on salicylic acid containing phenol and other foreign impurities.

Havenhill, L. D., also reports one sample as containing phenol.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

De Bruyn, Lobry, and Tijmstra (*Rec. Trav. chim.*, v. 23, pp. 385–393) discuss the mechanism of the synthesis of salicylic acid.—*Abstr. J. Chem. Soc. Lond.*, 1905, v. 88, pt. 2, p. 209.

Bigelow and Dubois read a paper (before the Am. Ass. Adv. Sc.) on the quantitative determination of salicylic acid, in which they attempt to define as exactly as possible the conditions to be followed in the estimation of salicylic acid: by extracting with solvents and comparing the color given with ferric chloride with that of solutions containing known amounts of salicylic acid. With the proper precaution it was suggested that results could be obtained which are reasonably correct.—*Exp. Sta. Rec.*, v. 17, No. 6, p. 612.

Harry and Mummery discuss the colorimetric estimation of salicylic acid in foodstuffs and outline a method for separating the salicylic acid in a state of purity, and determining the amount colorimetrically by the use of ferric chloride.—*Analyst, London*, 1905, v. 30, pp. 124–127.

Spica (*Gaz. chim. ital.*, v. 33, II, p. 482) outlines a method for detecting salicylic acid in wine, by converting it into picric acid and

coloring wool yellow with it.—Abstr. J. Am. Chem. Soc., 1905, v. 27, p. 1343.

Gorni, Felice, discusses the several methods proposed for the detection of salicylic acid in foodstuffs and outlines methods of procedure for detection of salicylic acid in wine, beer, milk, and butter.—Boll. Chim. Farm., 1905, v. 44, pp. 409-419.

Lloyd, John Uri, says that—

From the very introduction of salicylic acid as a medicine, the eclectic school in medicine selected the natural acid, made from wintergreen oil, and still adheres to the use of this preparation.—Pharm. Review, 1905, v. 23, p. 332.

Bondi and Jakoby (Hofmeister's Beiträge, v. 7, pp. 514-526), in studying the distribution of salicylic acid in normal and infected animals, find that the infected animals seem to eliminate salicylic acid more slowly than the normal.—Abstr. in Jahresb. (for 1905) ü. d. Fortschr. d. Tier-Chemie, Wiesb., 1906, v. 35, p. 125.

Baldoni, A. (Rendic. Soc. Chim. di Roma, 1905, v. 3), describes a new compound, salicylglycuronic acid, isolated from the urine after the administration of sodium salicylate.—Abstr., *ibid.*

Quenstedt reviews the literature and records his observations regarding the action of salicylates on the kidneys. He concludes that salicylates do not have a permanent deleterious effect on the kidneys; that salicylates are practically indispensable in acute cases of rheumatism, and that in chronic cases their use would not likely be continued, as they have little or no effect.—Therap. d. Gegenw., 1905, v. 7, pp. 97-100.

Frey, E., discusses the avoidance of irritation of the kidneys after large doses of salicylates. (Muench. med. Wchnschr., 1905, No. 28.)—J. Am. M. Ass., Chicago, 1905, v. 45, p. 745.

Ceroli, A., discusses the inconstancy of salicylates. (Gazz. d. Osp., Milano, v. 26, p. 28.)—Abstr., *ibid.*, p. 363.

Winkelmann, W. (Med. Klin., 1905, p. 730), believes that the administration of salicylic acid, intravenously, has no evident advantages over administration by mouth.—Apoth. Ztg., Berlin, 1905, v. 20, p. 516.

Brugsch, Theodor, reviews the work reported by Mendel, and its indorsement by Behr, and concludes that the intravenous injection of salicylates offers no distinct advantages over the internal administration of these compounds, and that, in addition, the disadvantages practically preclude the use of the former in private practice.—Therap. d. Gegenw., 1905, v. 7, pp. 63-64.

Mendel, F., reports some additional observations on the intravenous administration of salicylates and renews the assertion that he believes this to be the method of the future.—*Ibid.*, pp. 184-186.

ACIDUM SULPHURICUM.

Herting, Otto, discusses the nomenclature and tests for purity as compared with those included in the Ph. Germ., IV, and Ph. Brit., IV.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 127.

Lyons, A. B., points out that in the quantitative test, U. S. P., VIII, page 23—

It would be better to take 1 cc. of the acid for the titration rather than three. The latter would call for more than 100 cc. of the volumetric alkali. In general it may be remarked that the quantity of material prescribed for a titration should be such that between 20 and 30 cc. of the volumetric solution would be required. A smaller quantity necessitates very close readings of the burette.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 259.

Kebler, Lyman F., reports finding sulphuric acid containing lead and iron.—*Ibid.*, p. 182.

Burke, W. J., examined 25 samples of dilute sulphuric acid; 2 were practically of U. S. P. strength, 6 below, and 17 above; ranging from 7.05 to 19.4 per cent.—Proc. Massachusetts Pharm. Ass., 1905, p. 105.

Raschig, F. (Zeit. f. angew. Chem.), discusses the estimation of sulphuric acid.—Reprinted in Scientific Am. Suppl., 1905, v. 59, p. 24603.

Hart, Edward, in a review of some present problems in industrial chemistry, points out that sulphuric acid is now being made in quantity from the gases obtained in the roasting of zinc blende. Another source is in the roasting of pyrrhotite, of which vast deposits exist, among other places, in southwest Virginia.—J. Am. Chem. Soc., N. Y., 1905, v. 27, p. 158.

Luety, F., in a paper reprinted from the Zeitschr. f. angew. Chem., discusses the manufacture of sulphuric acid and describes some of the modern improvements in the sulphuric acid chamber process.—Chem. Eng., 1905-06, v. 3, pp. 25-32.

Raschig, F., discusses the several theories advanced as to the oxidation of nitrous oxide in the manufacture of sulphuric acid by the lead chamber process.—Ztschr. f. angew. Chem. 1905, v. 18, pp. 1281-1323.

Ferguson, W. C., publishes a sulphuric acid table which includes specific gravity determinations for sulphuric acid varying from 0.713 to 93.226 per cent.—J. Soc. Chem. Ind. Lond., 1905, v. 24, p. 787.

North and Blakey discuss the preparation of standard solutions of sulphuric acid. They review the several methods suggested in the last twelve years, and describe their method of preparing pure sodium bicarbonate, with tables of factors of acids obtained and of comparisons of bicarbonate as sold with pure bicarbonate.—*Ibid.*, pp. 395-397.

Scholtz, M., outlines a method for the titrimetric estimation of combined sulphuric acid. To a hot solution of the sulphate he adds

an excess of 1/10 N. barium chloride, and titrates this with a solution of potassium chromate. The excess of the chromate is subsequently determined by titration with sodium thiosulphate.—*Arch. d. Phar.*, 1905, v. 243, p. 667.

Lunge and Stierlen discuss the estimation of sulphuric acid in the presence of disturbing substances. They point out the limitations of the reaction between sulphuric acid and sulphates with barium chloride; also some of the possible sources of error.—*Ztschr. f. angew. Chem.*, v. 18, 1905, pp. 1921–1930.

Blacher and Koerber outline a simple method for the titrimetric estimation of the combined alkali sulphates by means of barium chloride with phenolphthalein and sodium carbonate as indicators.—*Chem. Ztg.*, Cöthen, 1905, v. 29, p. 722.

Linde (*Apoth. Ztg.*, 1905, pp. 46–47) has examined a number of drugs and finds that the color test for curcuma with sulphuric acid is fallacious. He records his experiments and enumerates a number of drugs that give a reaction similar to that given by curcuma.—*Abstr. Pharm. Zentralh.*, 1905, v. 46, p. 746.

Cook, George W., discusses the use of sulphuric acid in the removal of pulps with calcific formations.—*Dental Cosmos*, Phila., 1905, v. 47, p. 631.

Kuhl and Hahn (*Apoth. Ztg.*, 1905, v. 20, p. 867) discuss the composition of *mistura sulphurica acida* of the *Ph. Germ.*, IV, and point out that both this and the preparation of a similar character of the *Ph. Brit.*, IV, which is not so strong, undergo changes. He describes the methods recently devised for the examination of the German preparation and points out that up to a certain undetermined point there is production of ethyl hydrogen sulphate with a corresponding reduction in acidity.—*Abstr. in Pharm. J.*, Lond., 1905, v. 21, p. 723.

ACIDUM SULPHUROSUM.

Allen reports that he found samples of sulphurous acid which did not comply with the requirements of the official standard.—*Proc. Michigan Pharm. Ass.*, 1905, p. 80.

Ruff and Jeroch discuss the quantitative estimation of sulphurous acid in alkaline solutions, by titrating with iodine solution in an atmosphere of carbon dioxide in the presence of mannitol.—*Ber. d. deut. chem. Gesellsch.*, 1905, v. 38, pp. 409–419.

Blarez and Gautrelet report a study of the toxic action of sulphurous acid when injected subcutaneously.—*Bull. Soc. Pharm.*, Bordeaux, 1905, v. 45, pp. 169–177.

ACIDUM STEARICUM.

Francis, John M., points out that much of the commercial stearic acid has a melting point below 56° C. and should be refused, as a

difference of 2° or 3° will make a corresponding difference in the stability of the resulting glycerin suppositories.—Bull. Pharm., Detroit, 1905, v. 19, p. 317.

ACIDUM TANNICUM.

Francis, John M., calls attention to the fact that much inferior tannin is available and should be guarded against. He believes this inferior product to be made by some of the more economical processes and probably some cheaper solvent used in the final conversion of the substance into scales.—Bull. Pharm., Detroit, 1905, v. 19, p. 318.

Kebler, Lyman F., reports finding tannin which contained much resinous matter.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 182.

Thoms, H., reports a study of the tannins. He reviews the literature and the theories that have been advanced, reports some investigation into the composition of tannin and its relation to other compounds, and makes some suggestions upon the estimation of tannin.—Ber. d. pharm. Gesellsch., Berlin, 1905, v. 15, p. 303.

Virchow, C., discusses the precipitation of tannins by ammonium salts.—*Ibid.*, p. 348.

Trotman and Hackford (Chem. Ztg., 1905, p. 1189) suggest that, in place of the generally variable hide powder for the estimation of tannin, strychnine be used. They point out that a 1:10000 solution of tannin will still give a distinct reaction with the alkaloid strychnine.—Apoth. Ztg., Berlin, 1905, v. 20, p. 933.

Utz outlines a method for the valuation of tannin and records a series of experiments.—*Ibid.*, p. 907.

Williams, Walter S., outlines a method for the valuation of tannin from the view point of the dyer and calico printer. Among the several materials discussed are commercial tannic acid, sumach, catechu, and gambir.—J. Soc. Chem. Ind., Lond., 1905, v. 24, pp. 877-879.

Hommell, Philemon E., presents a tabulated list of drugs, official and non-official, which contain tannin, the parts of the plants which contain it, and, in a few instances, the percentage.—Proc. N. J. Pharm. Ass., 1905, pp. 61-66.

Winkel, Max, demonstrates that, contrary to the usual teaching, fruit—that is, the fleshy portion of fruit—contains considerable tannin in the form of a glucoside. From an aqueous extract of the fruit this substance is precipitated by powdered hide, solution of gelatin, and also by lead acetate.—Pharm. Post, Wien, 1905, v. 38, p. 358.

ACIDUM TARTARICUM.

Herting, Otto, discusses the origin and tests for tartaric acid and includes a table indicating a systematic method for the separation of oxalic, tartaric, citric, and malic acids.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 114.

Patch, Edgar L., reports finding one sample of tartaric acid which gave tests for copper and 20 samples which indicated the presence of iron and of sulphates beyond the U. S. P. limits.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

Voignier, Paul (*Rev. Chim. Indust.*, n. d.), discusses the manufacture of tartaric acid. The article contains considerable matter of general interest relating to the manufacture of tartaric acid, the analysis of argol, and the occurrence and origin of the raw material.—*Paint, Oil, and Drug Rep.*, 1905, Aug. 21, p. 24.

Ley (*Pharm. Ztg.*, v. 49, p. 149) outlines a method for the determination of tartaric acid.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 1340.

Cantoni and Zachoder (*Bull. Soc. Chim.*, v. 31, pp. 1121–1124) discuss the solubility in water of the tartrates of the alkaline earths. They point out that strontium is the most and barium the least soluble at the same temperature, and suggest that barium be used in the manufacture of tartaric acid, since the resulting salt is much less soluble than the corresponding salt of calcium, now generally employed.—*J. Chem. Soc. Lond.*, 1905, v. 88, Pt. II, p. 14.

ACIDUM TRICHLORACETICUM.

An editorial comment on the additions to the U. S. P., VIII, says that trichloroacetic acid is "much used as a test reagent for albumin and as a topical application, but there does not seem to be any special reason for including it in the pharmacopœia."—*Drug Topics*, 1905, v. 20, p. 195.

Riedel's *Berichte* points out that most authors, in common with the U. S. P., VIII, and the *Ph. Germ.*, IV, give a fixed boiling point for trichloroacetic acid, 195° C. The *Chemikerkalender* asserts that this acid boils at from 195° to 200° C., and some additional experiments recorded in Riedel's *Berichte* indicate that the boiling point, at 760 mm. pressure, is 197.3° C. It is suggested that a boiling point requirement of from 195.8° to 198.65° would meet all possible variations.—Riedel's *Berichte*, 1905, p. 43.

ACONITINA.

Herting, Otto, expresses some doubt as to the desirability of officially recognizing aconitine, particularly as the now official product is being marketed under the same name as others not at all identical with it.—*Deut.-Amer. Apoth. Ztg.*, 1905–6, v. 26, p. 155.

An editorial points out that the aconitines of commerce are so widely divergent that much care must be exercised when the dose exceeds $\frac{1}{100}$ grain. The official dose is $\frac{1}{400}$ grain.—*Drug Topics*, N. Y., 1905, v. 20, p. 196.

Dunstan and Andrews make several contributions to our knowledge of the aconite alkaloids: indaconitine, the alkaloid of *Aconitum chas-*

manthum; bikhaconitine, the alkaloid of *Aconitum spicatum*.—J. Chem. Soc., Lond., 1905, v. 87, part 2, pp. 1620–1636.

Cash and Dunstan (Proc. Roy. Soc., 1905, v. 76, pp. 468–490) report a pharmacologic study of the action of indaconitine and bikhaconitine.—Abstr. in Biochem. Centralbl., 1905–6, v. 4, p. 594.

Reichard, C. (Pharm. Zentralh., 1905, v. 46, pp. 479–486), discusses the reactions for aconitine and recommends a modification of the phosphoric acid test.—Pharm. Ztg., Berlin, 1905, v. 50, p. 562.

Alvarez (Bull. Commercial, 1905) describes an efficient method for the detection of aconite. He adds bromine, nitric acid, and alcoholic solution of potassium hydroxide to the substance to be tested, and when cool treats the resulting red-brown mass, which varies in depth of color, according to the amount of aconitine present, with 5 or 6 drops of a 10 per cent solution of copper sulphate; an intense green color results.—Am. Druggist, N. Y., 1905, v. 47, p. 98.

ACONITUM.

True, Rodney H., reports that aconite has been successfully grown in the testing garden of the U. S. Department of Agriculture.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 274.

An editorial objects to the requirement that aconite root should yield 0.50 per cent of total alkaloids by the U. S. P., VIII, method of assay, and points out that much more research is needed before a satisfactory assay of aconite is possible. “No assay is worth anything that does not determine the aconitine.”—Drug Topics, 1905, v. 20, p. 210.

Dohme, A. R. L., says aconite is now running much higher in aconitine than it did formerly, i. e., 0.80 per cent, in place of 0.50 per cent as required by the pharmacopœia. The average content for the past seven years varied from 0.55 per cent aconitine in 1899 to 0.92 per cent in 1902.—Apothecary, Boston, 1905, v. 17, p. 942.

Maben, Thomas, discusses standardization in the U. S. P., VIII, pointing out that some of the standards are surprisingly high, and that when the dose of aconitine and the dose of fluid extract of aconite are compared the surprise is not lessened.

The average dose of aconitine is $\frac{1}{400}$ grain; that of the fluid extract 1 minim, equal to $\frac{1}{300}$ grain. According to notions of dosage in this country this would be excessive, while that of the tincture is still worse, the dose being 10 minims, equal to $\frac{1}{200}$ grain aconitine. If any departure from the natural standard should ever be legitimate, I think aconite would have been a suitable case.—Pharm. J. Lond., 1905, v. 21, p. 140.

Caeser and Loretz outline a method for assay that provides for the extraction of the powdered drug with ether, using a 15 per cent solution of sodium hydrate as alkali. The ethereal solution is then treated with successive portions of 1 per cent hydrochloric acid; it is then

made alkaline with ammonia water and washed out with chloroform. The resulting solution is filtered, the chloroform distilled off, the residue dissolved in ether, and the latter evaporated. The residue is then dried in a dessicator to constant weight and weighed. For the titrimetric estimation the resulting material is to be dissolved in absolute alcohol, water added, and the resulting solution titrated with 1/10 N. hydrochloric acid, using hæmatoxylon as an indicator. Each cc. of the 1/10 N. acid equals 0.0645 gm. of aconitine.—Geschäfts Bericht von Caeser & Loretz, 1905, p. 102.

Holmes, E. M., discusses several species of Indian aconite root and makes some comparisons of the relative strengths of the aconitines.—Pharm. J., Lond., 1905, v. 21, p. 831.

Chevalier (Bull. gén. de Thérap., 1905, v. 150, p. 713) reports on a specimen of aconite obtained from North America, which, while morphologically identical with the official *Aconitum napellus*, contained 0.378 per cent of crystalline aconitine beside 0.580 per cent of amorphous alkaloid (japaconitine).—Biochem, Centralbl. 1905, v. 4, p. 715.

Senft, Em., describes and figures the structural characteristics of *Aconitum vulparis* Rehb. and of *Aconitum paniculatum* Lam. Fl. franc. ed. I. suppl. 1224.—Pharm. Prax., 1905, v. 4, pp. 445–460 and 495–502.

Truax, Florence T., in discussing the A, B, C of the Eclectic Materia Medica, says:

Aconite is sedative, stimulant, antiphlogistic, emmenagogue, anæsthetic; as a child's remedy unsurpassed.—Eclectic Med. J., 1905, v. 65, p. 534.

Francis, John M., deplores the omission of extract of aconite, and points out that this preparation has undoubted use in connection with the administration of aconite in the form of pills, and says:

We have personally examined hundreds of pounds of the extract which was possessed of full therapeutic potency.

He further points out that the official assay process does not determine pure aconite and that, consequently, the method of standardization is not so reliable as that proposed many years ago by Squibb.—Bull. Pharm., Detroit, 1905, v. 19, pp. 452, 496.

ADEPS.

Kebler, Lyman F., reports finding lard composed of 75 per cent of cotton-seed oil and 10 per cent of hard beef fat.

Wetterstroem, T., is quoted as reporting on 67 samples, of which number 27 were impure and 36 pure.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 185.

An abstract from the Helfenberger Annalen expresses the belief that the melting point of lard, as given in the Ph. Germ., IV, should

be raised somewhat, as an otherwise pure lard was found to require upwards of 47° C.—*Abstr. Pharm. Ztg.* Berlin, 1905, v. 50, p. 672.

Wesson and Lane discuss commercial lard and lard compounds, and outline the several tests that are useful or needed.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 714–717.

An abstract from the *Helfenberger Annalen* says that of 15 samples of lard examined, 5 were objectionable: 2 because of cotton-seed oil, and 1 because of an abnormally high percentage of water.—*Südd. Apoth. Ztg.*, 1905, v. 45, p. 521.

ADEPS LANÆ.

Francis, John M., calls attention to the fact that at the present time every conceivable quality of wool fat is being marketed, from the highest grade to a very crude "degras." Some of the lightest colored stock that he has seen was distinguished by a terribly offensive and persistent odor, which rendered it absolutely unfit for any salve or ointment.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 318.

Lifschütz, J., discusses the water absorbing properties of wool fat. (*Apoth. Ztg.*, v. 20, p. 857.)—*Pharm. J., Lond.*, 1905, v. 21, p. 723.

An abstract from *Seifensieder* discusses some of the uses of wool fat as a toilet article, its use in soaps, and in various creams designed for the prevention and cure of chapped skin.—*Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 9.

ÆTHER.

According to Riedel's *Berichte*, Schmitt and Beilstein give the boiling point of ether as being from 34.6° to 34.9° , and the experiments recorded by Riedel would also appear to indicate that the Ph. Germ., IV, requirement 35° C., certainly the U. S. P., VIII, requirement 35.5° C., is too high for an ether having a specific gravity of 0.720 at 15° C.—*Riedel's Berichte*, Berlin, 1905, p. 43.

Rossolimo, A. J., reports complications arising from the use of impure ether as a solvent in analytical work.—*Ber. d. deutsch. chem. Gesellsch.*, 1905, v. 38, pp. 774–775.

Ditz, H. (*Chem. Ztg.*, 1905, v. 29, pp. 705–710), points out that compounds, such as ethyl peroxide and hydrogen peroxide, are formed in ether on exposure to air, and that the use of such peroxide ether may produce unexpected phenomena when used as a chemical reagent. In illustration of this assertion the author recounts a number of experiments with various modifications of Kreis's reaction for decomposed or insolated fats.—*Abstr. J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 816.

An abstract calls attention to the statement that the contamination of ether with hydrogen dioxide is thought to be more frequent than

is generally supposed. It is best demonstrated by the yellow color produced with freshly prepared solution of potassium iodide.—Südd. Apoth. Ztg., 1905, v. 45, p. 758.

Becquerel, P. (Compt. rend. Acad. Sci. Paris, 1905, v. 140, pp. 1049-1052) has made a study of the action of ether and chloroform on dry seeds, and concludes that so long as the seed coat remains impermeable chloroform and ether are without effect.—Exp. Sta. Rec., v. 17, No. 6, p. 541.

Marble, Flora A., figures and describes a method for etherizing plants and forcing their subsequent growth in the living room of the house.—Exp. Sta. Rec., v. 17, No. 6, p. 563.

ÆTHER ACETICUS.

An editorial, in commenting on the U. S. P., VIII, commends the reduction in the standard for ethyl acetate content and expresses the opinion that the new requirements are more in keeping with the material now available.—Drug Topics, N. Y., 1905, v. 20, p. 210.

Kebler, Lyman F., reports finding a sample of acetic ether which contained calcium chloride.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 184.

ÆTHYLIS CHLORIDUM.

An abstract from the Lancet (Dec. 2, 1905, p. 1631) asserts that seven "makes" of ethyl chloride were obtained in the London market, and of these two were not labeled with the name of the maker. Five (one unbranded) were found to be pure; one from Francis Lepper (Ltd.) and one unbranded contained traces of impurity, but the former was not intended for general anæsthesia. One sample supplied as pure ethyl chloride consisted of a mixture of methyl chloride and ethyl chloride.—Abstr. in Pharm. J., Lond., 1905, v. 21, p. 869.

McCardie, W. J. (Lancet, Lond., 1905, Oct. 7), discusses the use of ethyl chloride, and believes it to be nearly, if not quite, as safe as ether for general use.—Abstr. in J. Am. M. Ass., Chicago, 1905, v. 45, p. 1449.

Murray, F. (Brit. M. J. Lond., 1905, November 25), regards the use of ethyl chloride as one of the best means of producing anæsthesia of from five to fifteen minutes in infants and older children. Reports a number of cases.—*Ibid.*, p. 1988.

Dalban, L., discusses the several uses and modes of employment of ethyl chloride in dental surgery.—Dental Cosmos, Phila., 1905, v. 47, pp. 402-403.

ALCOHOL.

An editorial expresses the belief that the U. S. P., VIII, requirements for alcohol are in keeping with the results of recent researches.—Drug Topics, 1905, v. 20, p. 210.

Vanderkleed, Charles E., reports that hundreds of barrel lots were examined during the year, and in almost every case the alcohol was found to be "up" in strength and purity. The government stamp, however, is not always a guaranty; two barrels showed a specific gravity of 0.8370 at 25° C., indicating only 81.3 per cent of absolute alcohol, by weight, instead of 91 per cent, as required (U. S. P., 1890).—*Proc. Penna. Pharm. Ass.*, 1905, p. 54.

Kebler, Lyman F., reports a sample of alcohol which contained organic matter and was excessively acid.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

Buchner and Meisenheimer discuss the process of fermentation by means of the extract of yeast cells, the substances produced, the production of alcohol from milk sugar; also some experiments on the production of acetic acid and of lactic acid by means of cell-free fermentation and some additional attempts to isolate other fermentation products.—*Ber. d. deutsch. chem. Gesellsch.*, 1905, v. 38, pp. 620–630.

Fleet, F. W., proposes the following procedure for deodorizing commercial alcohol:

Alcohol 95 per cent.....	fluid ounces..	28
Powdered quicklime.....	drachms..	4
Powdered alum.....	do.....	4
Spirit of nitrous ether.....	do.....	1

Mix the lime and alum, add the alcohol, and shake well, then add the spirit of nitrous ether, set aside for seven days, and filter through animal charcoal.—*Canad. Druggist*, Toronto, 1905, v. 17, p. 179.

Gaunt, R. (*Z. anal. Chem.*, 1905, v. 44, pp. 106–108), discusses the determination of alcohol in aqueous solutions by means of freezing and gives a table of the results obtained.—*J. Soc. Chem. Ind. Lond.*, 1905, v. 24, p. 294.

Duchmenin and Dourlen (*Compt. rend.*) have determined that alcohol is gradually oxidized in contact with air with the production of acetic acid. The acidity generally increases more rapidly in vessels of green color than in those of white glass.—*Pharm. Era*, N. Y., 1905, v. 34, p. 78.

Hartwich, C., discusses the widespread use of alcohol containing beverages and the nature and origin of some of the different compounds in which alcohol occurs.—*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 825.

An editorial comments on the universal craving for liquor and the efforts that are being made by unscrupulous manufacturers of proprietary medicines to supply the evident want in a surreptitious way.—*J. Am. M. Ass.*, Chicago, 1905, v. 45, p. 1409.

Kochmann, M. (from *Deut. med. Wchnschr.*, 1905, v. 31, pp. 942–944), discusses the action of alcohol on the circulation of man and concludes that alcohol raises the blood pressure, due to vaso-con-

striction in the domain of the splanchnic nerve, while there is vasodilation in the peripheral circulation.—Abstr., *ibid.*, p. 431.

Loeb, Oswald, reviews the literature bearing on the action of alcohol on the heart of warm-blooded animals and reports some experiments made to determine the effect of small doses.—Arch. f. exper. Path. u. Pharmacol., 1905, v. 52, pp. 459-480.

Bachem, C., reports some experiments made to determine the effect of small quantities of alcohol on blood pressure.—Arch. internat. de pharmacod. et de Thérap., 1905, v. 14, pp. 437-454.

Salant, W., expresses the belief that the experiments which he has conducted appear to indicate that moderate amounts of alcohol are helpful to digestion, while large amounts are injurious.—Exp. Sta. Rec., v. 17, No. 6, p. 613.

Friedenwald, Julius, discusses the pathologic effects of alcohol on rabbits and the effect of alcohol on the urine of rabbits.—J. Am. M. Ass., Chicago, 1905, v. 45, pp. 780-781.

Valentino, C. (Presse Méd., Paris, No. 73), reports some additional experiments on the action of alcohol on the brain and shows that its dehydrating effect appears to inhibit the absorption of strychnine and of snake venom.—Abstr., *ibid.*, p. 1205.

ALCOHOL, DENATURED.

A report of the departmental committee on industrial alcohol to the Chancellor of the Exchequer contains a section which deals with pharmaceutical products and fine chemicals, especially at the establishments of Merck and the Chemische Fabrik auf Actien, where the alcohol is denatured. The committee discusses the proposed regulations for the use of methylated spirit in Great Britain and the estimation of methyl alcohol.—J. Soc. Chem. Ind., Lond., 1905, v. 24, pp. 397-426.

Schmidt and Gaze discuss the detection of denatured alcohol in pharmaceutical preparations and give detailed directions for examining a number of preparations that may contain this adulterant.—Arch. d. Pharm., 1905, v. 243, p. 555.

Eschbaum, Schmidt, and Gaze contribute some additional reports on experiments made in connection with the detection of denatured alcohol in pharmaceutical products.—Pharm. Ztg., Berlin, 1905, v. 50, p. 1009.

Peters, R., discusses the detection of denatured alcohol in essences, tinctures, and fluid extracts.—Pharm. Zentralh., 1905, v. 46, p. 521.

Gadamer, J., discusses the detection of partially denatured alcohol in pharmaceutical preparations and figures the apparatus used.—Apoth. Ztg., Berlin, 1905, v. 20, p. 807.

Eschbaum, Friedrich, criticises the official (German) tests for denatured alcohol in spirituous preparations.—Ber. d. pharm. Gesellsch., Berlin, 1905, v. 15, p. 353.

Albert and Lythgoe discuss the detection and the determination of ethyl and methyl alcohols in mixtures by the immersion refractometer. They give several tables, including: percentage by weight of ethyl and methyl alcohols corresponding to scale readings on Zeiss immersion refractometer at 20° C.; scale readings on Zeiss immersion refractometer at 20° corresponding to each per cent by weight of ethyl and methyl alcohol; and readings with experimental mixtures of methyl and ethyl alcohols.—*J. Am. Chem. Soc.*, N. Y., 1905, v. 27, pp. 964-972.

Just's *Botanischer Jahresbericht* (for 1905, v. 33, part 3, p. 818) contains several references bearing on the production of alcohol and alcohol containing liquids.

ALCOHOL ABSOLUTUM.

Riedel's *Berichte* points out that the *Ph. Germ.*, IV, prescribes a boiling point of 78.5°C. for alcohol, regardless of the specific gravity. (The *U. S. P.*, VIII, prescribes 78°C. without qualifications.) Beilstein gives the boiling point of alcohol as 78.4°C. at a pressure of 760 mm. This figure agrees closely with the results of experiments recorded by Riedel, which show a variation of from 77.25° at 727 mm. pressure to 79.55° at 797 mm. pressure.—*Riedel's Berichte*, Berlin, 1905, p. 44.

An abstract (from *Ber.*, 1905, v. 38, pp. 3612-3616) discusses the preparation of pure ethyl alcohol and points out that the impurities to be removed from commercial absolute alcohol are aldehyde and 0.5 per cent of water. The aldehyde is removed by oxidation, by means of precipitated silver oxide in the presence of caustic alkali. The removal of water is effected by the action of metallic calcium, in the form of filings. The alcohol subsequently distilled should have a strength of 99.9 per cent. The author also includes a study of the specific gravity and the boiling point of pure alcohol, and remarks that the hygroscopicity of anhydrous alcohol has been somewhat exaggerated; 200 cc. of alcohol after standing exposed in an open beaker for fifteen minutes had not absorbed 0.1 per cent of water.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 1253.

ALOE.

Wilbert, M. I., points out that while the general heading "Aloe" allows the use of either Curaçao, Socotrine, or Cape Aloes, the first and most prominent chemical test of the *U. S. P.*, VIII, restricts the official drug to the one containing isobarbaloin. He points out several additional errors and shortcomings.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 343-348.

The committee on adulteration of the N. W. D. A. report receiving a communication which says in part:

We have had offered us, during the last year, by a number of brokers, a powdered aloes, so called, which contained only a trace of aloin. Investigation proved this to be an evaporated residue left after the extraction of the aloin from commercial aloes.—*Paint, Oil and Drug Rep.*, 1905, Oct. 6, p. 15.

The Ph. Hisp., VII, under the title aloes and the subtitle or synonym "*Aloe Soccotrina*," describes the drug obtained from various species of aloes and includes *Aloe vera* Mill., *Aloe spicata* Thunb., *Aloe ferox* L., *Aloe arborescens* Mill., *Aloe linguiformis* L., and others. It also includes sundry tests for solubility, purity, and identity.—*Farmacopea Oficial Española*, 1905, p. 45.

Leger, E., reports a further elaboration of his work on the aloes emodins.—*J. de pharm. et de chim.*, Paris, 1905, v. 22, p. 8.

Tschirch and Hoffbauer report additional studies on some of the more uncommon varieties of aloes, particularly of the aloin derived from them.—*Arch. d. Pharm.*, 1905, v. 243, p. 399.

Tschirch, A., discusses the oxymethylantraquinone drugs and their assay. Tabulated results of experiments with a number of drugs are given.—Reprinted in *Pharm. J.*, Lond., 1905, v. 21, p. 249.

The preceding papers are also abstracted in *Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 616-619.

van Itallie, L. (from *Pharm. Weekbl.*, 1905, No. 27), used the method described by Tschirch and Hoffbauer and compares several grades of aloes. He finds that Curaçao and Aruba aloes are not inferior to the Cape aloes, either in resin content or other requirement.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 835.

Fawcett, T. (*Pharm. J. Lond.*, v. 19, p. 401), discusses the detection and differentiation of aloes in compound rhubarb pills.—*Abstr. in Year Book Pharm.*, Lond., 1905, p. 227.

Francis, John M., believes that the use of the aloin in place of aloes, whenever permissible, is to be preferred. "The former may now be had of uniform quality, is readily obtainable, and is comparatively economical." He further believes that the use of aloin would be in keeping with the modern tendency toward concentration and small-sized doses.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 318.

Wilbert, M. I., points out that there is no longer any need for the continuance of purified aloes as a pharmacopœial preparation. He asserts that it is neither economical nor desirable, and that, as a matter of fact, it is not generally used in the making of pharmacopœial preparations, as directed.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 345.

ALONINUM.

Francis, John M., calls attention to the stress that is laid on the particular description of Curaçao aloin and suggests that if this

particular variety of aloin is superior, the others should not have been admitted; if not, no distinction should have been made. He also takes exception to the requirements that are made for aloin and believes that they are based on almost chemically pure material. The standard grades of aloin have a melting point of 130° to 142° C. and, on incineration, leave ash in amounts of from 0.11 to 0.40 per cent.—Bull. Pharm., Detroit, 1905, v. 19, p. 319.

The report of the committee on adulteration of the Michigan State Pharmaceutical Association asserts that as yet no aloin has been found that will comply strictly with the requirements of the pharmacopœia.—Proc. Michigan Pharm. Ass., 1905, p. 79.

Jowett and Potter (Pharm. J. Lond., 1905, p. 856) present a preliminary report on some work they have undertaken to determine the constitution of barbaloin. They are inclined to think that the formula for barbaloin, $C_{16}H_{17}O_9$, proposed by Tilden is more correct than the formula, $C_{21}H_{20}O_9$, more recently proposed by Leger.—Pharm. Zentralhl., 1905, v. 46, p. 880; see also Am. J. Pharm., Phila., 1905, v. 77, p. 901.

O'Connell, Charles J., points out that aloin produces a bright red color with many alkaloids, while with the salts of the same alkaloids little or no color is produced. This fact, he believes, confirms the suggestion that aloin has acid properties and tends to form salts or combinations with the several alkaloids.—Bull. Pharm., Detroit, 1905, v. 19, p. 294.

ALUMEN.

Pellet and Fribourg report a critical study of the several methods proposed for the determination of aluminum. They report on the methods by Carnot, Rivot, and Sainte-Claire-Deville.—Ann. de Chim. Analyt., 1905, v. 10, pp. 376–381.

Wadmore, J. M. (Chem. Soc. Proc., 1905, v. 21, p. 150), reports on sodium alum.—Abstr. J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 672.

AMMONII BROMIDUM.

Caspari, Charles E., examined 21 samples of ammonium bromide, only two of which complied with the pharmacopœial requirements. Thirteen contained an excess of ammonium chloride, probably due to the fact that the pharmacopœia permits less chloride in the ammonium bromide than in the corresponding salt of potassium or sodium. Four samples contained dirt and 6 metallic impurities.—Proc. Missouri Pharm. Ass., 1905, p. 75.

Gane is credited with finding a sample marked U. S. P. which assayed only 95.3 per cent of ammonium bromide.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 182.

Charteris, Frank, discusses the action of ammonium bromide and concludes that it is more toxic than sodium bromide. With large doses the predominating action is that of ammonium. The effect on the isolated frog's heart is not marked. With repeated non-toxic doses a bromide action may be produced.—*Therap. Gaz.*, Detroit, 1905, v. 29, pp. 722-726.

AMMONII CARBONAS.

Patch, Edgar L., found traces of chloride and sulphate in samples of ammonium carbonate.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

AMMONII CHLORIDUM.

Patch, Edgar L., is reported as having found ammonium chloride containing traces of aluminum and of copper.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 182.

An abstract from the monthly circular of Roessler and Hasslacher mentions a sample of ammonium chloride consisting of ammonium chloride, 49.97 per cent; sodium chloride, 44.6 per cent; sodium sulphate, 3.52 per cent; calcium sulphate, 1.55 per cent, and iron oxide, 0.09 per cent, the remaining portion being estimated as moisture.—*Drug Topics*, 1905, v. 20, p. 290.

Bauer, H. (*Pharm. Ztg.*, 1905), points out that because of the ready hydrolysis of ammonium chloride and of ammonium bromide in aqueous solutions, with the liberation of a corresponding amount of acid, the requirement of the Ph. Germ., IV, that solutions of these salts be neutral to litmus paper is not justified.—*Pharm. Prax.*, 1905, v. 4, p. 172.

Jean (*Ann. Chim. anal. appl.*, v. 9, p. 257) proposes a rapid titration for ammonium chloride and ammonium sulphate.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 1348.

Rupp and Rösler report on some experiments made to determine the availability of hypobromite solutions for the estimation of ammonia and of ammonium salts. It was found that free ammonia increases the alkalinity of the hypobromite solution and is not directly applicable.—*Arch. d. Pharm. Berlin*, 1905, v. 243, p. 104.

AMMONII SALICYLAS.

Schimpf, Henry W., asserts that ammonium salicylate is so little used that its introduction into the U. S. P., VIII, seems unnecessary.—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 514.

AMYLIS NITRIS.

Francis, John M., points out that a considerable portion of the amyl nitrite on the market is of an inferior grade, and some of it, from

reputable manufacturers, is not only worthless but absolutely a source of danger because of its lack of genuine amyl nitrite. The specifications of the pharmacopœia are quite elaborate, but, unfortunately, they will admit a poor, almost a spurious article. A safe and reasonable plan would be to demand that the liquid should assay at least 80 per cent by the process given, and, at the same time, 80 per cent of the total volume should distil off between 90° and 100° C. Amyl nitrite, it should be remembered, decomposes readily.—Bull. Pharm., Detroit, 1905, v. 19, p. 319.

Hare, Francis, discusses the use of amyl nitrite in several cases of hæmoptysis.—Therap. Gaz., Detroit, 1905, v. 29, p. 473.

Rand, W. H. (Am. Med., Apr. 29, 1905), records his experience with amyl nitrite in malaria. He says that it will often (not always) abort the seizure in its primary stage.—Merck's Rep., N. Y., 1905, v. 14, p. 214.

AMYLUM.

In an abstract it is pointed out that samples of "amylum tritici" were found which contained rice flour, while other samples were found to consist entirely of potato starch.—Südd. Apoth. Ztg., 1905, v. 45, p. 758.

Kraemer, Henry, reports some further observations on the structure of the starch grain.—Bot. Gaz., Chicago, 1905, v. 40, pp. 305-310.

Kraemer, Henry (from Science, 1905, v. 21, p. 504), points out that the starch grains of *Theobroma cacao* on heating may be made to assume forms that closely simulate the starch grains of corn, wheat, etc.—Biochem. Centralbl., 1905, v. 4, p. 535.

Fernbach and Wolff (Compt.-rend., 1905, v. 140, pp. 1547-1549) point out the analogy between starch coagulated by amylcoagulase and pea starch.—J. Chem. Soc., Lond., 1905, v. 88, Pt. II, p. 574.

Roux, E. (Compt.-rend., 1905, v. 140, pp. 440-442), discusses the transformation of amylocellulose into starch, and asserts that by incomplete degradation of amylocellulose he has produced artificial starches showing, under the microscope, cellular structures similar to those of natural starches, giving blue color with iodine, but not gelatinizing with hot water, and dissolving without residue in alkalies.—Abstr. J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 285.

Maquenne and Roux (Compt.-rend., 1905, v. 140, pp. 1303-1308) discuss the constitution, saccharification, and reversion of starch paste.—Abstr. in J. Chem. Soc., Lond., 1905, v. 88, Pt. II, p. 511.

ANISUM.

Spaeth, E., points out the need of calling attention to the adulteration of anise by extracting the valuable ethereal oil. Fruit that has been so extracted may be recognized by the unusually dark color

and the absence of the characteristic odor and taste. Italian fruit is frequently contaminated by the accidental admixture of conium. The anatomic structure of the seed should be included in official descriptions so as to facilitate the recognition of extracted fruit or of admixtures. A commercial anise should be required to consist of the undamaged anise fruit, not deprived in whole or in part of the ethereal oil, which has a strong odor and taste of anise. For air dry drug the limit of ash should be 10 per cent, and the hydrochloric acid insoluble ash should not exceed 2.5 per cent.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, 1905, v. 10, p. 21.

Hauke (in annual report of Philip Röder, Wien) suggests a permissible maximum ash content of 4 per cent for star anise seed. A sample of powdered star anise was found to contain 8.38 per cent of water and 1.81 per cent of ash.—*Pharm. Post.*, Wien, 1905, v. 38, p. 391.

ANTIMONII ET POTASSII TARTRAS.

Schwartz (*Giorn. d. pharm.*, 1905, p. 16) suggests that a saturated solution of antimony and potassium tartrate, when mixed with an equal volume of 1/10 N. thiosulphate solution, should remain clear for at least five minutes. The presence of potassium bitartrate is indicated by the separation of sulphur.—*Pharm. Zentralh.*, 1905, v. 46, p. 556.

For detection and determination of antimony in presence of organic matter see under Arsenic.

Vortmann and Metzl believe that they have simplified the method for the quantitative estimation of antimony, as trisulphide.—*Ztschr. f. analyt. Chem.*, 1905, v. 44, pp. 525–535.

ANTIPYRINA.

Francis. John M., points out that the expiration of the patent on antipyrine will undoubtedly lead to competition in manufacture and price, and this may result in some inferior goods being marketed. The tests supplied by the pharmacopœia will afford the pharmacist ample protection if he will apply them.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 361.

Siedler, P., asserts that the melting point given in the *Ph. Germ.*, IV, 113° C., is never reached, all of the available preparations melting at from 111° to 112° C.—*Pharm. Post. Wein.*, 1905, v. 38, p. 568.

Raikow and Külümow record a study of the action of Nessler's solution on antipyrine and give some account of the antipyrine oil produced.—*Oesterr. Chem. Ztg.*, 1905, v. 8, p. 445.

Bourat (*Bull. sci. pharm.*) describes a method for detecting as little as 2 per cent of antipyrine in pyramidon.—*Abstr. in Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 315.

Patein, G., outlines a method for the detection of antipyrine in pyramidon which depends upon the fact that antipyrine reacts with formaldehyde in the presence of hydrochloric acid to form diantipyrine methane, whereas pyramidon does not.—Abstr. in Pharm. J., Lond., 1905, v. 21, p. 361.

Lemaire, P., (Bull. Soc. Pharm., Bordeaux) has devised a method for the determination of antipyrine which depends on the fact that antipyrine combines with picric acid, forming an almost insoluble crystalline compound. A colorimetric method can also be used in the determination.—Abstr. in Analyst, London, 1905, v. 30, p. 22.

APOCYNUM.

Frye and Blodgett make a contribution to the life history of *A. androsamifolium*.—Bot. Gaz., Chicago, 1905, v. 40, pp. 49–53.

Lloyd, John Uri, points out that this American drug has been confused with its common namesake, the Indian hemp of India. The term Indian hemp, he believes, should be dropped and the name Canadian hemp employed, if a common name for it is necessary. The common name of apocynum (Indian hemp) refers to its use as a fiber plant by the aborigines of America, just as a common name of *Cannabis indica* (Indian hemp) connects it with the use of that fiber plant throughout the world.—Pharm. Review, 1905, v. 23, p. 298.

Rusby, H. H., believes that the indiscriminate use of several species of apocynum has discredited the drug and caused it to fall into disuse. When an active article is employed he believes it to be but little inferior to strophanthus.—Merck's Rep., N. Y., 1905, v. 14, p. 212.

Eberle, E. G., mentions apocynum among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Keys, Jerome, discusses the use of *A. cannabinum* in dropsy and obesity.—Abstr. in Hahneman. Month., Phila., 1905, v. 40, p. 397.

APOMORPHINÆ HYDROCHLORIDUM.

Francis, John M., points out that the specifications and the tests of the U. S. P., VIII, for apomorphine hydrochloride are complete, and that compliance with them should be insisted on. As this substance is prone to decomposition it should not be overstocked.—Bull. Pharm., Detroit, 1905, v. 19, p. 361.

Halle, Walter L., in a paper on the present status of our knowledge of morphine, discusses the structural formula for apomorphine and the relation of that substance to other derivatives of morphine.—Chem. Ztg., Cöthen, 1905, v. 29, p. 1267.

Pschorr, Robert (D. R. P. 158620), describes quarternary salts of apomorphine which are more stable and more readily crystalized than

the hydrochloride hitherto employed.—*J. Chem. Soc. Lond.*, 1905, v. 88, Pt. I, p. 638.

Baroni, E., discusses the preparation and the subsequent sterilization of solutions of apomorphine hydrochloride for hypodermic use.—*Boll. Chim. Farm.*, 1905, v. 44, pp. 597–599.

Richet, Ch. (From *Soc. Biol.*, 1905, v. 58, p. 958), reports observations on the anaphylaxis produced by injections of apomorphine.—*Abstr. in Biochem. Centralbl.*, 1905, v. 4, p. 286.

AQUÆ.

Caldwell, Paul, prefers the use of magnesium carbonate in the making of medicated waters.

The editor in commenting on this suggestion, points out that the presence of magnesium carbonate, in the resulting medicated water, may cause precipitation of alkaloids exhibited in the water thus prepared.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 306.

Williams, John R., suggests an improvement on the method of filtering medicated waters.—*Proc. Connecticut Pharm. Ass.*, 1905, p. 50.

AQUA.

Nixon, C. F., points out that in the U. S. P., VIII, aqua is defined as "potable water in its purest attainable state;" then we find that 500 parts of solids in 1,000,000 are allowable. "Such water," he asserts, "would be condemned by most boards of health. In aqua destillata, 75 parts in 1,000,000 are allowable, while most natural spring water in this section contains much less."—*Apothecary, Boston*, 1905, v. 17, p. 774.

An editorial comment on the U. S. P., VIII, discusses the official requirements for water and adds:

Mississippi, Schuylkill, and similar microbial consommés may therefore be employed, provided they stand the official tests.—*Drug Topics*, 1905, v. 20, p. 211.

Coblentz, Virgil, in discussing some of the comments that have been made on the U. S. P., VIII, says:

The apparent "inconsistencies" in aqua destillata are readily explained. Aqua is employed in making but comparatively few of our pharmacopœial preparations, and those instances where it is employed—fluid and solid extracts—the presence of 50 parts of total (inorganic) solids in 100,000 can and will not exert any deleterious effect, either on the preparation or the patient. Water is not condemned upon its solid (inorganic) content, but upon the nature of its impurities. The exclusion of water which contains nitrites, nitrates, chlorides, and ammonia in suspicious amounts is provided for more rigidly in the present pharmacopœia than in the former one for 1890. For distilled water due allowance should be made for the solvent action of distilled water on glass.—*Apothecary, Boston*, 1905, v. 17, p. 856.

Freyszinge and Roche (*Répert. de Pharm.*, 1905, p. 120) recommend the addition of from 0.03 to 0.05 gm. of calcium peroxide to 1 liter of water. Allow to stand for two hours and filter through manganese dioxide to destroy the resulting hydrogen dioxide. This treatment they believe will serve to sterilize infected or suspected water.—*Pharm. Zentralh.*, 1905, v. 46, p. 649.

AQUA DESTILLATA.

Ebert, K., points out that distilled water with a trace of copper in solution appears to have distinct advantages so far as keeping qualities are concerned. One sample observed by him was free from all evident contamination for a long period of time. While water containing copper may have the advantage of freedom from contamination, the author cautions against the use of such water in pharmacy.—*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 925.

AQUA AMMONIÆ.

Francis, John M., points out that this substance is very frequently contaminated with pyridine, which may prove very objectionable when the ammonia water is dispensed with other substances or used in manufacturing operations. If dilute sulphuric acid be added to ammonia water to a point just short of neutrality, pyridine, if present, will readily be detected by its characteristic odor. * * *

Pharmacists should note the legal possibilities involved in the specifications. "It (aqua ammoniæ) must not be dispensed for medicinal purposes if it contains less than 10 per cent by weight of the gas." Ammonia water loses its gas readily. Is your stock 10, 8, 6, or 2 per cent?—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 361.

Allen is reported as finding samples of ammonia water which did not comply with the requirements of the official standard.—*Proc. Michigan Pharm. Ass.*, 1905, p. 80.

Franklin, Edward Curtis, discusses the reactions that occur, or may occur, in liquid ammonia and contributes some further observations on the use of ammonia as a solvent.—*Ztschr. f. anorgan. Chem.*, 1905, v. 46, pp. 1–35.

Trillat and Turchet (*Bul. Soc. Chim.*, 1905, v. 33, pp. 304–308) have devised a new method for determining ammonia, which is based upon the fact that when iodine is brought in contact with ammonia a black precipitate or coloration, due to the formation of nitrogen iodide, is produced. This resulting coloration can readily be compared with standard solutions as in the Nessler test.—*Abstr. J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 458.

Bueler de Florin (*Chem. Ztg.*, v. 28, p. 1264) recommends the use of yellow glass plates instead of solutions of known ammonia con-

tent for a color scale in working with Nessler's reagent.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 1348.

Perman, E. P., records the results of attempts to synthesize ammonia with a view of determining whether there is a state of equilibrium between ammonia and its constituent elements at various temperatures. The author concludes that ammonia can not be synthesized by heat except under certain special conditions.—*Exp. Sta. Rec.*, v. 17, p. 525.

Ferguson, W. C., gives a table of specific gravities for ammonia water varying from 5.07 to 33.10 per cent of NH_3 .—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 786.

AQUA HYDROGENII DIOXIDI.

Patch, Edgar L. (*Am. Druggist*, 1905, p. 321), reports finding hydrogen dioxide solution containing 0.560 sodium arsenate per liter.

Wetterstroem, T., is reported as having examined four samples which assayed, respectively, 2.26, 3.25, 3.15, and 3.14 per cent: acidity 0.4 cc., 0.37 cc., 0.33 cc., and 0.33 cc., volume KOH.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 184.

The committee on adulteration reports that six samples were found to contain, respectively, 2.61, 2.96, 2.91, 4.41, 3.45, and 3.00 per cent of H_2O_2 .—*Proc. Michigan Pharm. Ass.*, 1905, p. 78.

Wetterstroem, Theo. D., in discussing the preservation of hydrogen dioxide points out that one-twentieth of 1 per cent of sulphuric acid is used to hold in check the hydrofluoric acid that trails into the preparation from the fluor spar, a contamination of the barium dioxide.—*Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 311.

Rumpel, H., in discussing the testing of medicinal hydrogen dioxide, expresses the belief that the apothecary is not sufficiently careful in testing his supplies of hydrogen dioxide. His results show that commercial samples require from 0.2 cc. to more than 2.0 cc. of normal potassium hydrate solution to neutralize the free acid contained therein. He believes that the test for free acid is much more valuable and more suggestive than the estimation of the contained H_2O_2 itself.—*Apoth. Ztg., Berlin*, 1905, v. 20, p. 984.

Grimbert, L. (*Journ. Pharm. Chim.*, 1905, v. 21), asserts that arsenic is frequently present in solutions of hydrogen peroxide. One sample recently examined gave a red precipitate on the addition of silver nitrate.—*Analyst, London*, 1905, v. 30, p. 208.

Schmatolla, Otto, in discussing the general subject of hydrogen dioxide, reviews the tests and the reactions for this compound.—*Pharm. Ztg., Berlin*, 1905, v. 50, p. 640.

Friend, John Albert, in discussing the estimation of hydrogen peroxide in the presence of potassium permanganate, points out that

correct titration may be made if (1) the titration be made with great rapidity; (2) the volume titrated be small; and (3) the concentration of sulphuric acid be fairly great.—*J. Chem. Soc., Lond.*, 1905, v. 87, pt. 2, pp. 1367-1370.

Planes, Paul (from *Journ. d. Pharm. et d. Chim.*), outlines a test for the colorimetric estimation of hydrogen dioxide which depends on the liberation of iodine from potassium iodide by free oxygen.—*Abstr. Répert. de Pharm.*, Paris, v. 17, p. 102.

Riesenfeld, E. H., discusses the decomposition of chromic acid by hydrogen peroxide.—*Ber. d. deutsch. chem. Gesellsch.*, 1905, v. 38, pp. 3578-3586.

Friedheim, Carl, presents some critical studies on the use of hydrogen peroxide in quantitative analysis, in the course of which he considers some of the criticisms that have been made by Jannasch on the use of hydrogen peroxide in the separation of manganese from zinc, manganese from copper, or chromium from aluminum.—*Ztschr. f. analyt. Chem.*, 1905, v. 44, pp. 388-392.

Baumann, E., reviews the literature relating to the preservation of milk by means of hydrogen peroxide and cites some of the objections that have been made to it; he records a number of experiments that were made to test the efficiency of the method, and concludes that every precaution should be taken to prevent contamination of the milk during milking, that milk should be treated immediately after milking before a multiplication of bacteria has taken place, and that a 30 per cent hydrogen peroxide solution can be used to avoid dilution of milk. (*Muench. Med. Wchnschr.*, 1905, pp. 1083-1088.)—*Exp. Sta. Rec.*, v. 17, No. 1, p. 74.

Eicholz (*Milchw. Zentralbl.*, 1905, v. 1, pp. 500-501), criticises the work of Baumann noted above.—*Ibid.*, p. 1006.

Vandevelde, A. J. J. (*Beitr. chem. Physiol. u. Pathol.*, v. 5, pp. 558-570), asserts that hydrogen peroxide increases the action of rennin, pepsin, trypsin, and the proteolytic ferments of milk. Variations in the effect of the reagent on the different ferments are discussed.—*Ibid.*, v. 16, p. 539.

Andresen, Vigo (*Deutsch. Monatschr. f. Zahnheilkunde*, Berlin, 1905), discusses the use of hydrogen peroxide in the treatment of sensitive dentine.—*Abstr. in Dental Cosmos*, Phila., 1905, v. 47, p. 402.

AQUA AURANTII FLORUM.

Francis, John M., points out that there is no means of determining the strength of orange flower water except "by the nose." Naturally, quality will vary with the price, and the pharmacist must rely upon his sense of smell and upon the probity of the supplier.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 361.

Goutal, B., calls attention to the adulteration of orange flower water by a distillate from the leaves and young shoots of *Citrus bigaradia* Risso. The author, failing in being able to distinguish the adulteration by chemical means, has studied various concentrations by the cryoscopic method and believes that it will be possible to develop a satisfactory basis for determining the purity of orange flower water by this means.—Bull. de pharm. du Sud-Est, 1905, v. 10, pp. 217-221.

ARGENTI NITRAS.

Baibakow, A. A., reports observations with 16 patients and believes that he is justified in concluding that the administration of silver nitrate tends to increase the motor activities of the stomach, lessen the content, and, in the majority of cases, at least, increase the total acid content. (From Russki Wratch, 1905, No. 31-33.)—Biochem. Centralbl., 1905, v. 4, p. 422.

An abstract from "Die neueren Arzneimittel" von Brückner Lampe & Co., enumerates the more widely used organic silver salts, such as actol, albargin, argentamin, argonin, collargol, ichthargan, itrol, largin, nargol, protargol, tachiol.—Deut.-Amer. Apoth.-Ztg., N. Y., v. 26, 1905, p. 67.

ARNICA.

Klobb, T., contributes some further notes on the phytosterol of arnica flowers, designated by him as arnisterin, and points out that it contains two OH groups, and he therefore proposes the name "arnidiol," to indicate its closer relations to the alcohols. (From Bull. des sc. pharm., 1905, No. 9.)—Pharm. Ztg., Berlin, 1905, v. 50, p. 846.

Fernald, M. L., discusses the occurrence of the genus *Arnica* in northeastern America.—Bull. Torrey Bot. Club, 1905, v. 32, p. 557.

y Guindal, J. M., describes some adulterants and substitutes for arnica root. (From Rev. Sci. de Barcelona.)—Proc. Am. Pharm. Ass., 1905, v. 53, p. 635.

La Wall, Chas. H., is reported as having found two samples of tincture of arnica containing wood alcohol.—*Ibid.*, p. 183.

Caldwell, Paul, suggests that in making tincture of arnica the drug be mixed with an equal weight of powdered pumice, moistened with sufficient of the menstruum, macerated for twenty-four hours, and finally exhausted by percolation in the usual way.—Drug., Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 306.

ARSENI IODIDUM.

Cowley and Catford, in discussing the description for arsenic iodide, say:

A pharmacopœia should give "sufficient" tests for purity. Not merely reference to methods of preparation but the best and most complete working formula should be given in detail.—Pharm. J., Lond., 1905, v. 21, p. 131. See also p. 217.

Saint-Philippe, R. (Bull. Acad. de Méd., Paris, 1905, v. 69, Nos. 39-40), reports his experience with the use of arsenic iodide in the treatment of scrofula.—Abstr. in J. Am. M. Ass., 1906, v. 46, p. 162.

ARSENI TRIOXIDUM.

Herting, Otto, calls attention to the differences in the Latin titles for arsenic trioxide. The U. S. P., VIII, title is *Arseni trioxidum*, the Ph. Germ., IV, *Acidum arsenicosum*, and the Ph. Brit., IV, *Acidum arseniosum*.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 127.

Herting, Otto, discusses the composition of arsenic trioxide and the tests included in the pharmacopœia.—*Ibid.*, p. 142.

Schimpf, Henry W., commends the change in name to Arseni trioxidum.—Am. J. Pharm., Phila., 1905, v. 77, p. 553.

Francis, John M., points out that the assay can be made more accurate by weighing out 1 gm. (instead of 0.1 gm.) of the substance, dissolving together with 10 gm. of sodium bicarbonate in 80 cc. of distilled water, then diluting this accurately to 100 cc. by the addition of water. Measure off 10 cc. of this solution, equivalent to 0.1 gm. of the original substance, and proceed with the titration as directed.—Bull. Pharm., Detroit, 1905, v. 19, p. 361.

Caspari and Suppan discuss the official method for the determination of arsenic, and outline several methods which they believe will give equally accurate results with a marked saving in time.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 320-323.

Heffter, A. (Arch. internat. de pharmacod. et de therap., v. 15, pp. 399-415), reports a study on the behavior of arsenic in the body. He finds in human urine after ingestion of arsenic by mouth 8 to 14 per cent, after injection subcutaneously 10 per cent, after intravenous injection 22 per cent, and after high rectal injection 1 per cent of the introduced dose. He also discusses the distribution of arsenic in the several organs of the body.—Abstr. in Jahresb. (for 1905) ii. d. Fortschr. d. Tier-Chemie, 1906, v. 35, p. 130.

Denigés, G., reviewing the work of Scolosuboff states (Bull. soc. de Pharm. de Bordeaux, 1905, p. 129) that he is in error; taking the muscle content as 1, that of liver as 1.8-2.0, that of the brain and spinal cord 0.4-0.7; these results are confirmed by those of Ludwig and Garnier.—Abstr., *ibid.*, p. 131.

Laveran, A., discusses the treatment of trypanosomiasis by means of arsenic and trypanroth.—Compt.-rend. Acad. d. sc. Par., 1905, v. 141, pp. 91-94.

ASAFETIDA.

Francis, John M., commenting on the U. S. P., VIII, requirements, says:

We almost feel like saying that we are not acquainted with this kind of asafetida.

He further suggests the substitution in the pharmacopœia of purified asafetida or asafetida resin, made by extracting the commercial drug with purified wood alcohol or alcohol, recovering the alcohol and evaporating the resin to extract consistence. Such a purified resin, he believes, would be of full strength and of uniform quality, and moreover would permit of smaller dosage, which is a great advantage in pills, tablets, etc.—*Bull. Pharm., Detroit, 1905, v. 19, p. 361.*

An editorial points out that the alcohol soluble content of the drug has been reduced to 50 per cent, but matters are evened up by placing a 10 per cent limit of ash. This will bar fully 50 per cent of what now passes the customs on a 60 per cent alcohol soluble content.—*Drug. Topics, 1905, v. 20, p. 211.*

Lloyd, John Uri, says:

Whilst this is not a favorite eclectic remedy it is used somewhat by certain physicians of the eclectic school. Be it said that, owing mainly to the mixture of sand and pebbles and other foreign substances, this drug is seldom if ever obtained in a condition to conform to all of the pharmacopœial requirements. It is a much abused remedial agent.—*Pharm. Review, 1905, v. 23, p. 298.*

Gane, E., is reported as finding asafetida containing 45 per cent of sand.

Patch, Edgar L., reports finding asafetida containing 62, 62.5, and 73.3 per cent of material insoluble in alcohol.—*Proc. Am. Pharm. Ass., 1905, v. 53, p. 183.*

Moore, Russell W., in discussing the quality of asafetida offered at the port of New York, says that tabulated results with two sets of samples tested in 1890 and 1900 show that in 1890 only 3.66 per cent of the samples examined were of the requisite purity, while in 1900 this had been increased to 14 per cent.—*Proc. Am. Pharm. Ass., 1905, v. 53, p. 265.*

The report of the revisors of the Vienna pharmacies (*Zeitschr. d. öesterr. Apoth.-Ver.*) points out that the residual ash of asafetida was found to vary from 20 to 30 per cent in eight samples, over 50 per cent in five samples, and over 60 per cent in two additional samples in place of the 10 per cent allowed by the pharmacopœia.—*Pharm. Prax., 1905, v. 4, p. 37.*

The report of the Belgian inspectors asserts that samples were found which contained as high as 75 per cent of ash.—*Bull. soc. roy. Pharm. Bruxelles, 1905, v. 49, p. 307.*

Gehe & Co. report that the importations of asafetida into London have increased from 608 cases in 1903 to 1,039 cases in 1904. The greater portion of this, however, was of inferior variety and there was comparatively little of the better quality of drug available.—*Handels Ber., Gehe & Co., 1905, p. 12.*

The report of the N. W. D. A. committee on adulteration quotes from a communication, as follows:

On analysis we have found no lot testing higher than 35 to 37 per cent of alcohol soluble material. It undoubtedly is necessary to add a small percentage of absorbing material, and in the drying of the gum the resin is oxidized to form alcohol insoluble compounds. Our conclusion is that powdered asafetida is unfit for pharmaceutical use and our laboratory has adopted a pure alcohol extract made from tears.—*Paint, Oil and Drug Rep.*, 1905, Oct. 6, p. 15.

Wetterstroem, Theo. D., has examined four samples of powdered asafetida which were found to contain from 20 to 33 per cent of alcohol soluble material. The ash was found to range from 50 to 60 per cent and was mostly inert earthy matter.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 312.

Vanderkleed, Charles, says that of eight samples of powdered asafetida examined one assayed 14.52 per cent of alcohol soluble material, one 23.5 per cent, and six others ranged from 27.28 to 33 per cent.—*Proc. Penna. Pharm. Ass.*, 1905, p. 54.

Douglass, Malcolm E., in notes on materia medica points out that asafetida is of use in hysteria, globus hystericus, diarrhœa, cardialgia, indigestion, hysteric asthma, and neuralgic rheumatism.—*Hahne-man. Month.*, Phila., 1905, v. 40, p. 202.

ASPIDIUM.

Rusby, H. H., believes that much less than one-half of the male fern sold in this country is really genuine, and that this may readily account for the lack of uniformity in its action that is so loudly complained of by physicians.—*Merck's Rep.*, N. Y., 1905, v. 14, p. 212.

The report of the revisors of Vienna pharmacies asserts that powdered "*Rhizoma filicis*" was found to contain powdered althæa leaves which had evidently been added to give to the drug the desirable light-green tint that a good quality drug of this kind should have.—*Pharm. Prax.*, 1905, v. 4, p. 38.

Kiczka, M., presents an exhaustive study of aspidium, with a report of the methods of procedure that were followed. Also reports an investigation of the composition of filicic acid, filicicacidbutanon, aspidinol and flavaspidic acid.—*Pharm. Prax.*, 1905, v. 4, pp. 96-102.

Caeser and Loretz outline a method for the estimation of crude filicin, which they believe to be indicative of the value of the drug.—*Geschäfts Bericht von Caeser & Loretz*, in Halle a. S. 1905, p. 85.

An abstract (from *Korr. Bl. f. Schweiz. Aerzte*) points out that E. Kraft has isolated a sixth substance from aspidium, which he has named "filmaron." It is a light yellow amorphous powder, which is readily soluble in acetone, chloroform, or ether, but is more difficultly soluble in alcohol, and is insoluble in water. Kraft found aspidium to contain 5 per cent filmaron, 3.5 per cent filicic acid, 2.5

per cent flavaspidic acid, 0.05 per cent albaspidin, and 0.1 per cent aspidinol.—Abstr. in Pharm. Ztg., Berlin, 1905, v. 50, p. 651.

Meyer, O. (Schles. Ges., 10, 1905), reports the case of a man (28) who, after a moderate (?) dose of oleoresin of aspidium, manifested marked symptoms of ocular disturbance and, on recovery from the acute condition, retained a marked impairment of sight.—Biochem. Centralbl., 1905-06, v. 4, p. 594.

Halbhuber (Sem. méd., 1905, p. 570) records his success in counter-acting by lemon juice the syncope following the administration of aspidium.—J. de pharm. et de chim., 1906, v. 23, p. 114.

ATROPINA.

Herting, Otto, discusses the composition of atropine, its uses, and its relation to hyoscyamine.—Deut.-Amer. Apoth. Ztg., 1905, v. 26, p. 156.

Siedler, P., points out that the Ph. Germ., IV, directs that atropine sulphate should have a melting point of 180° C. When the directions of the pharmacopœia are followed the melting point will run up to from 186° to 190° C. Under ordinary conditions and with some care 185° to 186° will suffice, and only with the exercise of great care can this substance be melted at 180° C.—Pharm. Post, Wien, 1905, v. 38, p. 568.

Reichard, C. (from Chem. Ztg., v. 28, p. 1048), discusses the relation of atropine and morphine and outlines a number of tests and reactions that are characteristic of these two alkaloids.—Pharm. Zentralh., 1905, v. 46, p. 554.

An abstract (from Bull. Imp. Inst., II, 4, 1905, pp. 222-223) discusses the alkaloidal content of *Hyoscyamus muticus* from Egypt, and suggests the use of this drug as a source for both hyoscyamine and atropine.—Just's Bot. Jahresb., 1905, P. III, v. 33, p. 189.

Petrow, W. I. (Dissert., St. Petersburg, 1905), in discussing the decomposition of various alkaloids by the different organs of the body, points out that because of the readiness with which atropine is destroyed it is practically impossible to secure positive results.—Biochem. Centralbl., 1905, v. 4, p. 495.

Drenkhahn records some experiences with the use of atropine in gynecology. He reports several cases and makes some suggestions as to the use of this alkaloid.—Therap. Monatsh., 1905, v. 19, pp. 57-61.

Spurgin, Percy B. (Lancet, Lond., 1905, ii, pp. 964), reports two cases of poisoning from the application of atropine to the eyes.—Merck's Archives, 1905, v. 7, p. 364.

Meyer, A. (Corr. Bl. f. Schweiz. Aerzte, Basel, 1905, v. 35, pp. 548-550), makes a contribution on the fatality of atropine intoxications.—Reference from Ind. Med., 1905, p. 1052.

Löble, W. (Wien. klin. Wchnschr., 1905, v. 18, pp. 888-889), discusses poisoning with atropine.—Reference from *Ind. Med.*, 1905, p. 1052.

Doyen and Kareff (Bull. Soc. méd. d. hôp. de Lyon) discuss the action of atropine on the liver and the coagulability of the blood.—Reference from *Ind. Med.*, 1905, p. 788.

AURI ET SODII CHLORIDUM.

Goldschmidt, Carl, points out that gold may be quantitatively separated from solutions, either in the presence or absence of other metallic salts, by simply boiling the solution in a nickel or a nickel amalgam dish. The gold separates out as a brownish powder.—*Pharm. Zentralh.*, 1905, v. 46, p. 735.

BALSAMUM PERUVIANUM.

Francis, John M., in a review of the U. S. P., VIII, says, under balsam of Peru:

Sufficient attention has not been paid to the quality of this balsam. The pharmacopœial specifications will enable the pharmacist to protect himself if he will take the trouble to insist on their compliance.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 362.

Wiebelitz (from the laboratory of Diedr. Buchmann) believes that the upper limit (1.150) for the specific gravity of balsam of Peru, allowed by the Ph. Germ., IV, is too low. He has found otherwise excellent balsam having a specific gravity of 1.154 and upwards and believes that the upper limit might well be placed at 1.155.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 779.

Caeser and Loretz point out that in view of the increasing production of the so-called "synthetic balsam of Peru" it becomes more necessary to apply the available tests. They believe the sulphuric acid test to be unreliable and superfluous. The odor and the saponification and ester numbers are important. They also recommend the nitric acid test, practically as given in the U. S. P., VIII.—*Geschäfts Bericht von Caeser & Loretz*, in Halle, a. S., 1905, pp. 9-78.

Gehe & Co. report a liberal supply of excellent balsam of Peru and point out that the so-called "synthetic balsam" is not of satisfactory quality. Even apart from its nonconformity with the physical tests, this synthetic product could not be construed as being acceptable under the provisions of the Ph. Germ., IV, as that book clearly defines the origin and the method of obtaining balsam of Peru.—*Gehe & Co., Handels-Bericht*, Dresden, 1905, p. 13.

Hellström, A., presents a comprehensive study of a sample of white balsam of Peru, with an introduction embodying many interesting historical and pharmacognostic notes.—*Arch. d. Pharm.*, 1905, v. 243, p. 218.

Tschirch and Bueckhardt contribute a preliminary report on an investigation of a sample of white balsam of Peru. This new product, they believe, is not identical with the so-called "white balsam of Peru" obtained from the seeds of *Myroxylon pereira*. It belongs to the substance known as "styrax balsams."—Pharm. Post, Wien, 1905, v. 38, p. 570.

Thoms and Biltz examined a sample of white balsam of Peru, discuss the constants and characteristics of the several fractions obtained by distillation.—Arb. a. d. Pharm. Inst. d. Univer. Berlin, 1905, v. 2, pp. 127–131.

Flückiger and Mauch (J. de Pharm. d'Anvers, 1905, p. 128) discuss the detection of gurjun balsam, in balsam of Peru and in copaiba, by the nitrosulphuric acid reaction applied to a sample dissolved in carbon disulphide. They believe that this reaction is not conclusive unless applied to the essential oil distilled from the balsam.—Abstr. in Chem. & Drug., Lond., 1905, v. 67, p. 70.

Aufrecht (Pharm. Zentralh., 1905, p. 887) examined artificial balsam of Peru and found that it resembles the true article in many particulars but differs from it in that the saponification and iodine numbers are materially different. The natural balsam usually has an average saponification number of 239, and an iodine number of 55. The synthetic product was found to have a saponification number of 206 and an iodine number of 33.7.—Pharm. Post, Wien, 1905, v. 38, p. 782.

The report of inspectors of pharmacies in Belgium mentions the finding of balsam of Peru having a low density and adulterated with storax, gurjun balsam, and turpentine.—Bull. Soc. roy. Pharm., de Bruxelles, 1905, v. 49, p. 307.

Sorber, Alblas (Pharm. Weekbl., 1905), points out that the addition of a small quantity of castor oil to ointments containing balsam of Peru and other substances will tend to prevent the granulating tendency that is frequently found in these ointments. Castor oil contains little or no triolein, and this is thought to be the direct cause for the separation so frequently noted with mixtures containing balsam of Peru with oils and fats.—Pharm. Ztg. Berlin, 1905, v. 50, p. 1023.

Bischoff (Apoth. Ztg.) asserts that a perfect ointment containing balsam of Peru may be obtained by the use of carnauba wax. The incompatibility may be overcome by first rubbing down the boric acid or any other medication with a little castor oil. This is then mixed with the fat or petrolatum and the balsam added afterwards.—Year Book Pharm., Lond., 1905, p. 231.

Deutsch (Ztschr. f. Med. Beamte, 1905, p. 409) reports that three children had been treated, at the suggestion of a quack, with inunctions of vinegar, soap, and balsam of Peru. All three developed

signs of poisoning and one, a boy, died of acute nephritis.—Pharm. Zentralh., 1905, v. 46, p. 805.

Schloffer (Arch. f. klin. Chirur., v. 77, No. 3) discusses the treatment of infected wounds by the local application of balsam of Peru.—Therap. Gaz., 1905, v. 29, p. 784.

Douglass, Malcolm E., in notes on materia medica, points out that balsam of Peru is useful in the treatment of mucopurulent discharges, cough after pneumonia, indolent ulcers, and cracked nipples.—Hahneman Month., Phila., 1905, v. 40, p. 205.

BALSAMUM TOLUTANUM.

Francis, John M., points out that in the purchase of balsam of tolu special care should be exercised to obtain a light-colored article, as it is practically impossible to produce a nice, water-white syrup of tolu if the balsam is not light colored. For the dark preparations light balsam is of course not essential.—Bull. Pharm., Detroit, 1905, v. 19, p. 362.

An abstract from Roeder's Report outlines the method for determining the acid number of balsam of tolu, as follows:

One gm. of the balsam is dissolved in 20 cc. of chloroform, then diluted with from 150 to 200 cc. of neutral alcohol and titrated with $\frac{1}{4}$ N KOH solution with phenolphthalein as an indicator. The number of cc. of alkali used, times 14, gives the acid value. According to K. Dietrich this should be between 114.8 and 158.6; the Ph. Germ., IV, permits 112 to 168.—Year Book of Pharmacy, Lond., 1905, p. 13.

Williams, John K., suggests that a solution of balsam of tolu, that will be of use in making other preparations, can be made by dissolving one part of the balsam in sufficient alcohol to make two parts.—Proc. Connecticut Pharm. Ass., 1905, p. 52.

Astruc and Cambe discuss the preparation of syrup of balsam of tolu and suggest the use of granulated balsam, which is directed to be prepared by making a 10 per cent solution of balsam in alcohol and pouring this upon clean sand in a mortar. After thorough trituration the product is exposed to air, with occasional stirring to prevent agglomeration; it may be preserved in well-closed bottles. For the syrup, 5 parts of this granulated balsam is treated with hot water and the sugar dissolved in the resulting solution.—Year Book of Pharmacy, Lond., 1905, p. 157.

BELLADONNA.

Francis, John M., feels certain that more or less scopolia is being consumed for belladonna, and reports having seen a consignment of 15 bales of belladonna which consisted of from 15 to 20 per cent of scopolia. In this connection, too, he points out that official belladonna

consists of the dried leaves, while the commercial drug frequently consists almost entirely of the whole plant, tops or branches with stems unremoved, the latter constituting a large part of the total weight. As regards belladonna root, he points out that enormous quantities of scōpola root have been used to replace belladonna root in the manufacture of plasters, and that such a procedure appears to be generally indorsed or at least condoned. He also calls attention to the substitution of poke root for belladonna.

Speaking of the use of inferior drugs in the making of standardized preparations, he says:

While, theoretically, an increased quantity of poor drug will make a good fluid extract, if the latter be standardized by assay, there are, however, practical objections to using an excessive quantity of drug, as the fluid will be highly charged, with extractive matter, and will not keep well.—Bull. Pharm., Detroit, 1905, v. 19, p. 362.

Rusby, H. H., reports that he has seen a large importation of belladonna root of which at least a quarter consisted of some inert root, apparently wild althæa, or a relative of that plant.—Merck's Rep., 1905, v. 14, p. 212.

True, Rodney H., reports that belladonna has been successfully grown for a number of years in the testing gardens at Washington.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 274.

Maben, Thomas, in discussing the question of standardization in the U. S. P., VIII, asserts that the standard for belladonna leaves is in accordance with what has long been recognized as a fair average. He questions the reliability of the term "dried," and suggests that this be more accurately defined.—Pharm. J., Lond., 1905, v. 21, p. 140.

Vanderkleed, Charles E., examined 13 samples of belladonna leaf, which assayed from 0.181 to 0.437 per cent of alkaloid. The samples assaying low were characterized by a large proportion of stem. Five samples of belladonna root were analyzed and found to vary from 0.42 to 0.60 per cent of alkaloid.—Proc. Penna. Pharm. Ass., 1905, p. 55.

Dohme, A. R. L., asserts that the variation in the alkaloidal content of belladonna leaf has been small indeed for the seven years 1899–1905. The minimum content in 1899 and 1900 was 0.42 per cent, while the maximum, 0.46 per cent, was found in 1901, 1903, and 1904. Belladonna root varied from 0.68 per cent of alkaloids, found in 1901, to 0.5 per cent in 1902.—Apothecary. Boston, 1905, v. 17, p. 942.

Henderson, H. John, discusses the percentage of alkaloid in belladonna root, and gives a tabulated statement of the percentage of extractive and of total alkaloids found in lots of 800 or 900 pounds each. He also gives the results of analysis of 30 samples of foreign root.—Pharm. J., Lond., 1905, v. 21, p. 191.

Caeser and Loretz outline a method of assay for belladonna in which the alkalized drug is directed to be extracted with ether instead of a mixture of ether and chloroform as directed in the U. S. P., VIII. The process is suggested for both gravimetric and titrimetric estimation.—Geschäfts-Bericht von Caeser & Loretz, in Halle a. S. 1905, p. 88.

Dietrich, K. (Helfenberger Annalen), points out that there is much danger of inaccurate results in the assay of belladonna leaves and of hyoscyamus, unless the presence of chlorophyl is taken into consideration. The green tint of the extract makes it difficult to recognize the change in color when titrating with iodeosin as an indicator.—Pharm. Ztg., Berlin, 1905, v. 50, p. 672.

Naylor, W. A. H., points out that considerable economy of time and labor may be effected by subjecting the extract of belladonna to a preliminary treatment for the removal of its fat. He discusses several methods that have been proposed and recommends Bird's modified Ph. Brit., IV, process.—Pharm. J., Lond., 1905, v. 21, p. 124.

Gadd and Gadd, in discussing the testing of drugs and chemicals by dispensing chemists, outline a ready process for the assay of alkaloids in the liquid extract of belladonna, Ph. Brit., IV.—*Ibid.*, p. 438.

Farr and Wright discuss powdered alcoholic extracts of belladonna leaf and root and give their findings.—*Ibid.*, v. 20, pp. 398 and 546; Abstr. in Year Book of Pharm., Lond., 1905, pp. 232-238.

Dulière, Walter, discusses the application of the method of assay for extract of belladonna as given in the Ph. Germ., IV, and points out that chlorophyl acts as a disturbing factor.—Ann. de Pharm. de Louvain, 1905, v. 11, pp. 185-191.

Forsberg, W. C. (Pharm. Post, v. 38, p. 2), discusses the determination of the alkaloids in belladonna leaves and suggests the use of sodium carbonate as the alkali and subsequent extraction with a mixture of ether and chloroform.—Abstr. Year Book Pharm., Lond., 1905, p. 46.

Truax, Florence T., in an article on the A B C of the Eclectic Materia Medica, characterizes belladonna as a stimulant of the highest character, invaluable in the treatment of all wrong life where the slow pulse, dusky colored skin, and cold extremities denote blood stasis and capillary congestion * * * chronic diarrhoea or dysentery, chronic constipation, kidney derangement, or menstrual irregularity.—Eclectic Med. J., 1905, v. 65, p. 536.

Douglass, Malcolm E., in notes on materia medica, says of belladonna:

With the single exception of opium there is probably no single medicine so important as belladonna in existence. For internal use atropia is danger-

ous. At first the dose should not exceed $\frac{1}{100}$ of a grain; but subsequently it may be increased with caution to $\frac{1}{30}$ of a grain and in special (poison) cases even to $\frac{1}{10}$ grain.—Hahnemann. Month., Phila., 1905, v. 40, p. 371.

See also under "Therapeutic uses."—*Ibid.*, pp. 509-520.

BENZALDEHYDUM.

Francis, John M., points out that probably the use of benzaldehyde will be an advantage when the uncertain quality and the instability of the natural oil is taken into consideration, but care must be exercised to obtain a properly refined article. The pharmacist should remember to test for "chlorinated products."—Bull. Pharm., Detroit, 1905, v. 21, p. 362.

In an editorial note on the U. S. P., VIII, it is pointed out that the official product is required to be free from chlorine, a requirement rather difficult to comply with, as most of the commercial samples contain rather more than 0.2 per cent of chlorine. It is possible to obtain a chlorine-free product, however, at an enhanced price.—Drug Topics, 1905, v. 20, p. 196.

Umney and Bennett, in discussing benzaldehyde estimation, point out that this is not likely to give identical results in the hands of different operators. The end reaction is not sharp, and comparable results will only be obtained by practice.—Pharm. J., Lond., 1905, v. 21, p. 145.

Bourquelot and Danjou (J. d. pharm. et. chim., 1905, p. 154) have discovered a glucoside in the leaves, blossoms, and fruit of the common elder, *Sambucus nigra* L., yielding benzaldehyde. They outline the method employed in extracting the glucoside.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.-Nov., pp. 110-111.

BENZINUM.

Raubenheimer, Otto, refers to the confusion which exists between the terms benzine, naphtha, and gasoline, and defines these names and the substances to which they are properly applicable. Hydrometer 60-69 B. means benzine, usually 62 B.; Hydrometer 70-79 B. means naphtha, usually 76 B.; Hydrometer 80-89 B. means gasoline, usually 86 B.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 428.

Bridtman (Pharm. Ztg.) discusses the inflammability of benzine. He finds that a mixture of 7 volumes of carbon tetrachloride and 3 volumes of benzine is still inflammable upon the approach of a match, and that only when the proportion of 9 of the former to 1 of the latter is reached does the liquid require heating before it ignites.—Abstr. Pharm. Era, 1905, v. 34, p. 556.

BENZOSULPHINIDUM.

Francis, John M., points out that competition has led to very cheap prices for saccharin (sold under various names), and that as

a consequence it is not all of the same quality. He further asserts that there is no excuse for the pharmacist purchasing an inferior grade if he will use the tests supplied in the U. S. P., VIII.—Bull. Pharm., Detroit, 1905, v. 19, p. 362.

An abstract (Ztschr. f. Unters. d. Nahr. u. Genussm., 1905, p. 245) points out that adulterated saccharin, particularly in the form of tablets, is not uncommon in Austria. Tablets have been found that were largely composed of plaster of Paris sprinkled over with saccharin; others contained less than 1.6 per cent of saccharin.—Abstr. Pharm. Ztg., Berlin, 1905, v. 50, p. 845.

Koehler (Pharm. Ztg., Berlin, 1905, v. 50, p. 227) asserts that the gradual decrease of sweetening power of saccharin tablets is due to excess of the alkali bicarbonate present, also to the fact that much of the commercial so-called bicarbonate is really the very alkaline sesquicarbonate.—Abstr. Pharm. J., Lond., 1905, v. 21, p. 230.

An editorial quotes the above statements and adds the comments of manufacturers who assert that saccharin tablets do not lose their sweetness under ordinary conditions, and that they continue to contain their original amount of saccharin even after a long period.—Am. Druggist, N. Y., 1905, v. 47, p. 4.

v. Mahler, E. (from Chem. Ztg.), bases a test for saccharin on the property of metallic sodium or potassium combining with the sulphur of compounds containing it to form sulphides on fusion.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 17.

Kastle, J. H., proposes a color test for saccharin which involves heating the substance with a mixture of 5 cc. of phenol and 3 cc. of concentrated sulphuric acid. When small quantities of saccharin are heated with small amounts of this mixture to 160°–170° C. for five minutes and the mass dissolved in a small amount of water and rendered alkaline with 2 N sodium hydroxide, the solution becomes dark purplish red or pink, depending on the amount of the saccharin present. He points out that any great excess of the reagent is to be avoided and that the best results are obtained with the smallest amount of the reagent that it is practicable to use.—Bull. No. 26, Hyg. Lab. U. S. P. & M.-H. S., 1906, pp. 31–33.

Procter, C. (Chem. Soc. Trans., 1905, v. 87, pp. 242–249), discusses the determination of saccharin (benzoyl sulphonie imide). Confirming Reid's process, he finds that saccharin and para-saccharin liberate iodine quantitatively from a solution containing potassium iodide and iodate and proposes a method for determining the two compounds.—Abstr. in J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 515.

Beringer, George M., discusses the average dose and believes it to be in excess of that generally given.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 415.

Mathews and McGuigan discuss methods for determining the condition in which saccharin leaves the body. In discussing the influence of saccharin on the digestive enzymes they assert that saccharin has a retarding influence on the digestive juices, especially that of the saliva and pancreas.—*J. Am. M. Ass.*, Chicago, 1905, v. 45, p. 844-847.

Sternberg, William, discusses the sweetening properties of the dulcines and records some experiments made to determine the comparative sweetness of the several compounds.—*Riedel's Berichte*, 1905, p. 54.

BENZOINUM.

Francis, John M., points out that of 22 consignments of benzoin, composed of 60 odd cases, 7 assayed between 80 and 90 per cent and 10 between 70 and 80 per cent of alcohol soluble matter, the average being 80.4 per cent, the highest being 92 and the lowest 38 per cent. In the major portion of these samples the ash was in excess of the permissible 2 per cent. He does not believe that his experience is unique in this respect.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 362.

Garner, J. Bert (*Am. Chem. J.*, v. 32, pp. 583-606), discusses the reaction between benzoin and alcoholic potassium hydroxide, enumerates the findings of Zinin, Jena, Limpricht, Schwanert, Owens, and others, and proposes an elaboration of the experiments of Papcke, who uses a solution of sodium ethoxide.—*Abstr. J. Chem. Soc.*, Lond., 1905, v. 88, Pt. II, p. 143.

Meisenheimer, Jakob (*Ber.*, 1905, v. 38, pp. 874-878), does not concur in Garner's results.—*Ibid.*, p. 291.

BERBERIS.

Francis, John M., points out that berberis varies tremendously in quality and from time to time tons of it, of very inferior quality, almost devoid of the peculiar bitter, yellow substance are offered. He has not been able to determine whether such drug is obtained from an allied plant or whether its inferiority is due to collection at the wrong season. A good drug can always be distinguished by its deep yellow color.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 362.

Lyons, A. B., points out that the definition for berberis is defective in that it permits of the use of any species of berberis in place of *Berberis aquifolium*. The word "certain" before "other" would have been more explicit, but even this should have some limitation, such as "indigenous in the States of the far west" or belonging to the sub genus mahonia.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

Douglass, Malcolm E., in notes on materia medica, points out that berberis is useful in acne, scaly diseases, psoriasis, pityriasis, etc., and in syphilis.—*Hahneman. Month.*, Phila., 1905, v. 40, p. 748.

BETANAPHTHOL.

Lemaire, P., enumerates the several characteristics of the two naphthols and of the methods and tests best suited for their differentiation.—Bull. Soc. Pharm., Bordeaux, 1905, v. 45, pp. 230-242.

Riedel's Berichte reports some investigations as to the boiling point of betanaphthol and notes variations in current literature. The new determinations would appear to indicate that the boiling point of this substance, at 760 mm. pressure, is about 296° C.—Riedel's Berichte, Berlin, 1905, p. 47.

Edlefsen, G., reports a study of betanaphthol, its elimination and the demonstration of its presence in the urine after ingestion of naphthalin, benzonaphthol, and betanaphthol.—Arch. f. exper. Path. u. Pharmacol., 1905, v. 52, pp. 429-458.

BISMUTHUM.

The reviewer of the U. S. P., VIII. points out that the term "bismuthum" is objectionable in view of the fact that well-known scientists have agreed on wismut and bismutum without the h.—Pharm. Ztg., Berlin, 1905, v. 50, p. 701.

von Lippmann, Edward C., in a contribution to the history of bismuth, expresses the belief that the salts of this metal were known and used in the arts as early as the fourteenth century.—Chemiker Ztg., Cöthen, 1905, v. 29, p. 719.

Belavoine (Chem. Ztg., 1905, p. 333) discusses the several methods proposed for the quantitative estimation of bismuth and points out their defects. He asserts that good results may be obtained by reduction with formaldehyde, the only objection being that the finely divided precipitate is readily oxidized on exposure to air. The most satisfactory results have been obtained by the electrolytic precipitation in the form of a bismuth-mercury amalgam, the objection to this method being that a minute error in the estimation of the mercury will materially change the accuracy of the results.—Pharm. Zentralh., 1905, v. 46, p. 555.

Miller and Cruser (J. Am. Chem. Soc., 1905, v. 27, pp. 116-121) discuss the application of bismuth ammonium molybdate to gravimetric analysis and particularly to the development of a gravimetric method for the estimation of bismuth.—Abstr. J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 292.

Hollard and Bertiaux discuss the estimation of bismuth in the presence of other metals, particularly of copper and of lead. They also outline a method for separating these substances by means of electrolysis.—Ann. de chim. analyt., Paris, 1905, v. 10, p. 11.

Reichard (Pharm. Prax.) outlines a method for detecting traces of bismuth, in the presence of antimony, by the use of brucine or its

sulphate. A drop of a concentrated solution of chloride of bismuth placed in a porcelain capsule and a fragment of brucine, or a drop of concentrated solution of brucine added, yields a bright red color.—*J. de pharm. d'Anvers*, 1905, v. 61, pp. 67–68.

BISMUTHI SUBGALLAS.

Francis, John M., points out that competitive reduction in price has led to the sale of inferior products, of a dull or brownish color, containing impurities. The most objectionable of these impurities he considers to be free gallic acid, and points out that a sample of a fine bright yellow color will seldom be found open to criticism.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 363.

BISMUTHI SUBNITRAS.

Francis, John M., calls attention to the rather marked differences in specific gravity or density of samples of bismuth subnitrate from different manufacturers, and thinks that the pharmacist would be surprised if he would weigh equal measures of different brands. He further points out that the light bulky subnitrate, while it comes a little higher in price, is probably worth the difference for dispensing purposes.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 363.

Caspari, Chas. E., examined 31 samples, but 2 of which conformed rigidly to the U. S. P. requirements; 29 contained chloride, 4 contained ammonium salts, and 1 contained free acid. The small amount of chloride present is doubtless harmless, and it is evident from its frequent occurrence that its complete removal is attended with considerable difficulty, so that a limit might be placed on chloride in bismuth subnitrate instead of prohibiting it entirely. The ammonium salts emanate from the ammonium carbonate or hydrate used by some in precipitating the subnitrate, and they should be washed out completely.—*Proc. Missouri Pharm. Ass.*, 1905, p. 75.

Crouzel, Ed., discusses the reason for the manifestation of ammonia on triturating a bismuth subnitrate with calcined magnesia.—*Ann. de chim. analyt.*, 1905, v. 10, pp. 349–350.

Bonz and Son found a sample of bismuth subnitrate with an appreciable admixture of tellurium. They suggest that the Swiss Pharmacopœia include the stannous chloride test of the Ph. Germ., IV, so as to provide for such a possible contamination.—*Pharm. Zentralb.*, 1905, v. 43, p. 530.

Douglass, Malcolm E., in notes on materia medica, points out that bismuth subnitrate is one of the most valuable remedies for external application; it is also useful in gastrodynia, dyspepsia, headache, etc.—*Hahneman. Month.*, Phila., 1905, v. 40, p. 753.

BROMOFORMUM.

Francis, John M., points out that the products of decomposition of bromoform are very irritating, so that carelessness may result in producing just the opposite of the effect that is desired. In view of this fact, he believes that it is hardly necessary to warn pharmacists that purchases should be for limited quantities of this article and that they should assure themselves of the purity and freshness of the product when obtained. For this purpose the tests most essential are those with silver nitrate and with potassium iodide and starch.—Bull. Pharm., Detroit, 1905, v. 19, p. 363.

Riedel's Berichte points out the need for a revision of the boiling point of bromoform, as a sample examined began to boil far below the minimum temperature given in the Ph. Germ., IV, 148° C.—Riedel's Berichte, Berlin, 1905, p. 45.

Schoorl and Van den Berg make a preliminary report on some experiments that have been made to determine the influence of air and light on bromoform.—Ber. d. pharm. Gesellsch., Berlin, 1905, v. 15, p. 405.

Roth (Rev. méd. lég., Paris, 1905, p. 243) reports a fatal case of poisoning, by bromoform, in an infant.—Reference from Ind. Med., 1905, p. 1052.

BROMUM.

Cormimboeuf, H., discusses the detection of bromine in large quantities of iodine, and outlines a method for the detection of bromine in iodides, hydriodic acid, and also in free iodine.—Ann. de Chim. analyt., Paris, 1905, v. 10, pp. 145-146.

Stroud, H. E. (Surg. Gynec. & Obst., Chicago, 1905, v. 1, pp. 530-533), discusses the antiseptic action of bromine, with descriptions and illustrations of cases.—Reference from Ind. Med., 1906, p. 63.

BUCHU.

Francis, John M., calls attention to the change that has been made in the composition of the menstruum for fluid extract of buchu, and doubts the expediency of this change unless made on conclusive experiments. He has failed to find anything in print which would appear to warrant the change to the use of so weak a menstruum in the extraction of a drug which owes its activity to an oleoresin or a camphoraceous body.—Bull. Pharm., Detroit, 1905, v. 19, p. 496.

An abstract (credited to Chem. & Drug.) calls attention to a new buchu which has appeared on the London market. The leaves are round or oval, with entire instead of serrated margins, of a leathery consistency, and with many oil glands. The leaves make an aromatic mucilaginous infusion similar to that of *Barosma betulina*, the

official buchu. The ethereal oil is a semi-solid with a distinct odor like that of peppermint, and contains diosphenol. The botanical identity of the leaves has not been determined.—*Ibid.*, p. 521.

CAFFEINA.

Reichard, C., reviews the tests and reactions applicable to caffeine.—*Pharm. Zentralh.*, 1905, v. 46, p. 846.

Siedler, P., points out that the Ph. Germ., IV, requires a melting point of 230.5° C. When caffeine is dried as directed in the pharmacopœia he finds that it requires a temperature of 234° : when dried in the air bath the melting point may be as high as 236.5° . The air dry substance melts at 229° C.—*Pharm. Post, Wien*, 1905, v. 38, p. 568.

Puckner, W. A., in discussing the estimation of caffeine records some experiments made to determine the conditions under which caffeine may be dried without loss. He also reports on the estimation of caffeine in the presence of acetanilide, and presents the details of a series of experiments which led to the adoption of a process in which the caffeine is precipitated as a periodide.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 285-289, 292-298.

Waentig, J. Percy, presents a study of the several methods for the determination of caffeine. He concludes that the method proposed by J. Katz gives the most satisfactory results with roasted coffee.—*Arb. a. d. kais. Gesundheitsamte, Berlin*, 1905, v. 22, pp. 315-332.

Bertrand, Gabriel, describes several varieties of coffee which contain little or no caffeine. These coffees come from Madagascar, in the neighborhood of La Grande Comore, and have been identified as being the product of *Coffea gallienii*, *C. bonnierii*, and *C. mogeneti*. In addition to these three, *Coffea humboltiana*, also from the same neighborhood in Madagascar, has been described.—*Compt-rend. Acad. d. sc., Paris*, 1905, v. 141, pp. 209-211.

Petrow, W. I. (Dissert., 1905, St. Petersburg), reports some observations on the destruction of caffeine, strychnine, and atropine in the several organs and concludes that caffeine is destroyed in relatively large quantities, particularly in the liver.—*Biochem. Centralbl.*, v. 4, 1905, p. 495.

Schwabe, G. (*Arch. Ophthalmol.*, July, 1905), discusses the influence of caffeine on the field of vision in quinine amblyopia.—*Abstr. in J. Am. M. Ass.*, 1905, v. 45, p. 497.

Loewi, O. (from *Sitzungsberichte d. Gesellsch. z. Beförd. d. ges. Naturw. z. Marburg*, 1905, pp. 76-79), discusses the nature of the diuresis produced by caffeine.—Reference from *Ind. Med.*, 1905, p. 675.

Zilinski, W. (*Wratschebnaja Gazeta*, 1905, No. 35), in discussing the influence of convallamarin, strophanthin, and caffeine on the

isolated mammalian heart finds that caffeine increases the work of the heart and strengthens the heart contractions. The number of contractions per minute is increased but the nutrition of the heart is decreased.—*Biochem. Centralbl.*, v. 4, 1905, p. 495.

Douglass, Malcolm E., suggests the use of caffeine in cardialgia, spasmodic asthma, hemicrania, and nervous palpitations; it is a direct heart stimulant. "Used in sleeplessness and drowsiness; lithaemic conditions and uraemic coma." Caffeine Citratis Effervescens is a most pleasant method of administration.—*Hahneman. Month., Phila.*, 1905, v. 40, p. 851.

CAFFEINA CITRATA.

"A junior Pharmacist" in "Notes on official galenicals" suggests the use of much less than the *Ph. Brit.* IV quantity of distilled water. He suggests dissolving 1 pound of citric acid in 10 fluid ounces of water, then adding the caffeine and evaporating.—*Pharm. J., Lond.*, 1905, v. 21, p. 462.

Francis, John M., believes that the new formula for effervescent citrated caffeine owing to the omission of the sugar is a decided improvement.—*Bull. Pharm., Detroit*, 1905, v. 19, p. 363.

CALAMUS.

Eberle, E. G., mentions calamus among the medicinal plants found in Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 304.

Francis, John M., considers the menstruum for the official fluid extract of calamus weak in alcohol.—*Bull. Pharm., Detroit*, 1905, v. 19, p. 496.

CALCII CARBONAS PRÆCIPITATUS.

Lyons, A. B., points out that—

No titration test is given, although such tests can be very easily made. There is no test given for the common impurity of magnesium, but this omission may have been intentional.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

Patch, Edgar L., reports finding precipitated carbonate of calcium containing 2.1 per cent of material insoluble in dilute acids, and another sample containing sand, iron, and chloride.—*Ibid.*, p. 183.

CALCII CHLORIDUM.

Stokes, H. H., reports the use of calcium chloride in two cases of hæmorrhage, with apparent good results.—*Brit. M. J., London*, 1905, i, p. 183.

Godfrey, Jas. M., reports a case of hæmophilia treated with calcium chloride.—*Hahneman. Month., Phila.*, 1905, v. 40, pp. 126–128.

CALCII HYPOPHOSPHIS.

Havenhill, L. D., examined a sample of calcium hypophosphite which was found to be very impure.—*Proc. Kansas Pharm. Ass.*, 1905, p. 91.

CALCII PHOSPHAS PRÆCIPITATUS.

Ilhardt, W. K., found a sample of precipitated calcium phosphate contaminated with iron and chloride.—Proc. Am. Phar. Ass., 1905, v. 53, p. 183.

Cameron and Seidell investigated the composition of the solutions of solids resulting when phosphates of calcium are brought into contact with water. So-called tri-calcium phosphate yields an acid solution, the amount of phosphoric acid formed depending upon the original composition of the sample and the relative proportions of solid and water used.—J. Am. Chem. Soc., 1905, v. 27, pp. 1503-1512.

Cameron and Bell present the results of some additional work on the same subject.—*Ibid.*, pp. 1512-1514.

CALCII SULPHAS.

Sullivan, E. C., determined the solubility, at 25° C., of calcium sulphate in ammonium sulphate solution. Presents a tabulation of his results.—J. Am. Chem. Soc., 1905, v. 27, pp. 527-539.

Cameron and Brown discuss the solubility of calcium sulphate in solutions of other salts, including those of sodium chloride, nitrate, and sulphate: magnesium chloride and nitrate and ammonium chloride and nitrate.—(From J. Phys. Chem., v. 9, pp. 210-215.) *Ibid.*, p. 387.

CALENDULA.

Eberle, E. G., mentions calendula as being one of the medicinal plants found in Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Mundy points out that calendula is specifically indicated by an enfeebled condition of the capillary blood vessels, cracked nipples, catarrhal condition of nose and throat, varicose ulcer, and suppurative disease of the middle ear.—Eclectic M. J., 1905, v. 65, p. 349.

CALUMBA.

An abstract (from Pharm. J., Lond.) points out that Alcock found a sample of calumba which, on incineration, yielded 16 per cent of ash. Wardleworth believes that the drug is the product of *Tinospora bakis*. Holmes, on the other hand, believes that the fictitious drug is the overground portion of the root of *Jateorrhiza calumba* itself.—Pharm. Zentrall., 1905, v. 46, p. 670.

Francis, John M., asserts that practical experience with the fluid extract of calumba leads him to believe that the more concentrated menstruum of perhaps 80 to 85 per cent of alcohol, by volume, will yield a fluid extract of better appearance and one which will keep better than that prepared with the official menstruum.—Bull. Pharm. Detroit, 1905, v. 19, p. 528.

CALX.

Lyons, A. B., in discussing "Calx" says:

No quantitative test is proposed. None is really needed—neither is the purity requirement of 90 per cent needed—as it is to be made from white marble or from the purest varieties of calcium carbonate.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 261.

Kebler, Lyman F., found calcium oxide which contained siliceous matter, aluminum, iron, and chloride.—*Ibid.*, p. 183.

Bunge (*Ztschr. f. Biol.*, v. 45, pp. 532-539) records the content of calcium oxide and of iron found in the several substances used as food.—*Nouv. Rem.*, 1905, v. 21, pp. 91-94.

CALX CHLORINATA.

Francis, John M., speaking of the titration of chlorinated lime, says:

It would seem that the insoluble lime residue interferes in some way with the titration and the process will be improved by allowing the 1,000 cc. of aqueous solution to stand for a few minutes, then decanting and titrating, as directed, 100 cc. of the clear supernatant solution. Of 23 consignments, amounting to over 30,000 pounds, all assayed over the U. S. P., VIII, minimum requirement. The highest was 38.5 per cent and the lowest 30.4 per cent and the average 34.4 per cent of available chlorine. Chlorinated lime deteriorates rapidly and care must be exercised in purchasing small quantities and in observing that requisitions be not filled from old stock.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 363.

Kebler, Lyman F., publishes the following figures on chlorinated lime:

Samples in tins, 21 per cent to 26 per cent. Fresh goods, 33 per cent to 37 per cent, and one sample of American manufacture, 42 per cent.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 185.

The committee on adulterations reports one sample of chlorinated lime which contained but 12.6 per cent of available chlorine instead of the 30 per cent required by the U. S. P.—*Proc. Michigan Pharm. Ass.*, 1905, p. 78.

Alcock, F. H., found that six samples of chlorinated lime varied in content from 15.9 to 30.1 per cent of available chlorine. He suggests that—

an addition of quicklime might tend to preserve it, or, as it has been shown that the soda chlorinata keeps better, an admixture of some sodium salt.—*Pharm. J. Lond.*, 1905, v. 21, p. 520.

Smith, Bernard F., reports an investigation of commercial samples of bleaching powder in which he shows that even under the most favorable conditions this article will deteriorate more or less rapidly. The writer concludes that the purchaser should insist upon getting

a fresh article.—*Proc. Ass., Off. Agr. Chem.*, 22 Ann. Conv., (1905) 1906, pp. 33–35.

Pontius (*Chem. Ztg.*, v. 28, p. 59) determined the active chlorine in bleaching powder, etc., by using the principle that hypochlorous acid in the presence of primary sodium carbonate oxidizes iodide to iodate. He added the chlorinated lime solution to some primary sodium carbonate in a dish, then some starch paste and titrated with potassium iodide solution till the next drop caused no blue color.—*Abstr. J. Am. Chem. Soc.*, 1905, v. 27, p. 1347.

Tarugi, N., discusses the formation and the constitution of bleaching powder (from *Gaz. chim. Ital.*, 1905, v. 34, p. 254–260, 466–468). He attributes the pink coloration of bleaching powder to the presence of iron, probably in the form of calcium ferrate. The iron cannot be determined by the permanganate method.—*Abstr. J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 25, 332.

Reuter, L., discusses the chemistry of bleaching powder and the reactions involved in its production.—*Pharm. Rev.*, 1905, v. 23, p. 125.

Gehe & Co. point out that, of the 260,000 tons of chlorinated lime produced in 1904, fully one-half was produced by the electrolytic method. The United States produces practically no chlorinated lime by the older Leblanc method.—*Gehe & Co. Handels-Bericht*, 1905, p. 12.

CALX SULPHURATA.

Lyons, A. B., believes that the U. S. P., VIII, requirement of 60 per cent [later reduced to 55 per cent] of calcium sulphide, in calx sulphurata, is too stringent. That of the Ph. Brit., IV, 50 per cent, he thinks reasonable.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

Ryan, J. J., tested 16 samples of calx sulphurata, the percentage of calcium monosulphide varied from 10 to 60 per cent; three, or 18.75 per cent of the samples, corresponded to the U. S. P. requirements.—*Proc. Massachusetts Pharm. Ass.*, 1905, p. 104.

CAMPHORA.

Timberlake, A., reviews the history of camphor, its production and the methods of purification; he also refers to other closely related products.—*Proc. Indiana Pharm. Ass.*, 1905, pp. 95–101.

True, Rodney H., points out that camphor trees have been successfully grown in Florida, Southern California, Texas, etc. These trees, it is asserted, yield a satisfactory quantity of crude gum when properly distilled.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 273–274.

Kimberlin, E. M. (*Am. Druggist*, v. 46, 1905, p. 315) describes some of the camphor trees growing in California and discusses the

possibility of developing an industry in this connection.—Abstr. *Ibid.*, p. 623.

The Bureau of Plant Industry reports that the fresh leaves and twigs of trees grown in Florida contain from 1.0 to 1.5 per cent of camphor.—Ann. Rep. Dept. Agriculture, 1905, pp. 149.

Gehe & Co. report that crude camphor was difficult to obtain and that, for a considerable period of 1904, practically no crude material was being exported from Japan. They also discuss synthetic camphor and outline the several methods that are being developed for its production.—Gehe & Co. Handels-Bericht, Dresden, 1905, p. 15.

An abstract, discussing the value of camphor trees, points out that every part of a camphor tree, even to the leaves, contains camphor. Among the by-products are crude camphor oil, white oil, red oil, and a turpentine which is obtained from the white oil.—Pharm. Era, N. Y., 1905, v. 34, p. 127.

Francis, John M., asserts that we have not, as yet, reached the era of successful camphor manufacture, but that it is only a matter of time and that, therefore, the subject of proper identification tests should receive attention.—Bull. Pharm., Detroit, 1905, v. 19, p. 363.

Kremers, Edward, gives an account, with illustrations, of the method of collecting and marketing Borneo camphor.—Pharm. Review, 1905, v. 23, p. 7.

An unsigned article describes the several methods now known or being developed for the synthetic production of camphor. These are designated as: 1, Portchester Chemical Co.'s process; 2, J. C. Richardson's process; 3, E. Schering Chemical Co.'s process.—Bull. Soc. Roy de Pharm. de Bruxelles, 1905, v. 49, p. 136.

Sautermeister, C., presents a discussion of the chemical constitution of camphor and reviews the attempts that have been made to produce it synthetically.—Südd. Apoth. Ztg., 1905, v. 45, pp. 353-355, 361-363.

Richardson, J. C. (Chem. and Drug., v. 65, p. 850) discusses the prospects of synthetic camphor. He concludes that the synthetic product can only compete seriously when it is possible to make a considerable reduction in the price of the crude material and cheapen the cost of manufacture.—Schimmel & Co. Semi-Ann. Rep., 1905, Apr.-May, p. 118.

Gössling, W., reviews the work that has been done in connection with the synthetic production of camphor.—Pharm. Post, Wien, 1905, v. 38, p. 599.

Brandel, I. W., presents some observations, from the current literature, on the source and composition of camphor oil.—Pharm. Review, 1905, v. 23, p. 380.

Schimmel & Co. discuss the addition products obtained from the safrol of camphor oil, and the behavior of these addition products

with different reagents.—Schimmel & Co., Semi-Ann. Rep., 1905, April–May, pp. 13–19.

“B.” points out that a sample of spirit of camphor that he prepared had a specific gravity of 0.8848, in place of from 0.885 to 0.889 as required by the Ph. Germ., IV. To induce the separation of camphor required the addition of 5.5 cc. of water in place of from 4.6 to 5.3 cc. The alcohol used had a specific gravity of 0.8322, and on further examination it was found that the camphor melted at from 172° to 173° , or from 2° to 3° lower than specified in the pharmacopœia.—Pharm. Zentralh., 1905, v. 46, p. 526.

Caldwell, Paul, suggests preparing camphor liniment by heating the oil to about 88° C. and pouring this upon the camphor contained in a suitable flask or can. Cork well and shake until the camphor is dissolved.—Drug. Circ. & Chem. Gaz., N. Y., 1905, p. 220, v. 49.

Cook, E. F., presents an assay method for the examination of camphor liniment.—Proc. N. J. Pharm. Ass., 1905, pp. 76–80.

Lothian, J., suggests that the following requirement be added to the official test: “5 gm. heated in a flat-bottomed dish for one hour on the water bath should lose not less than 1 gm.”—(From Pharm. J., Lond., v. 20, p. 582.) Abstr. Year Book Pharm., Lond., 1905, p. 55.

A formula for camphorated chloral is given as follows: camphor, 2 parts; phenol, 1 part; mix.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 1356.

An editorial states that the Druggists' Circular for December, 1874, page 203, contains a reprint of an article from the London Medical Record, describing the production and uses of camphorated phenol. Two years later (Drug. Circ., March, 1877, p. 54) there was published an abstract of a paper by Soulez along the same lines.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 280.

v. Chlumsky (Centralbl. f. Chirurgie, 1905, v. 32) is enthusiastic over the fine results obtained from the use of carbolic acid and camphor in the treatment of wounds.—Abstr. J. Am. M. Ass., Chicago, 1905, v. 45, p. 1453.

Böhme, Arthur, discusses the influence of camphor on the frog's heart, under varying conditions.—Arch. f. exper. Pathol. u. Pharmacol., 1905, v. 52, pp. 346–369. Also, monograph published by J. B. Hirschfeld, Leipzig, 1905. 28 pp., 8vo.

Gottlieb, R. (from Ztschr. f. exper. Path., 1905, v. 2, p. 385), reports some observations on the action of camphor on the heart of the dog.—Biochem. Centralbl., v. 4, 1905, p. 494.

Mayer (Münch. Med. Wchnschr., v. 52, p. 42) reports his experiences with Pirogoff's method of treating erysipelas with camphor.—Abstr. J. Am. M. Ass., 1906, v. 46, p. 79.

Seligmann, E., reports some observations made to determine the action of camphor on the circulation.—Arch. f. exper. Path. u. Pharmacol., Leipz., 1905, v. 52, pp. 333-345.

Löbke, W. (Wien. klin. Wchnschr., 1905, v. 18, pp. 886-888), reports on cases of poisoning by camphor.—Reference from Ind. Med., 1905, p. 1052.

Boericke, William, discusses the use of camphor in cholera, coryza, convulsions, etc.—Tr. Am. Inst. Homœop., 1905, v. 61, pp. 390-395.

CANNABIS INDICA.

Vanderkleed, Charles E., examined 11 samples of cannabis indica which were found to contain from 7.05 to 16.2 per cent of resin, the standard for good drug being taken as 10 per cent. Some of the samples running low were admittedly not grown in the East Indies.—Proc. Penna. Pharm. Ass., 1905, p. 55.

Lloyd, John Uri. The adulterant of cannabis indica, or rather the substitution sold for it, is the American-raised plant, which differs in quality so materially from the same plant raised in its native country as to have earned for it the term *Cannabis sativa*, to which the name "Indian hemp" should not be applied.—Pharm. Review, 1905, v. 23, p. 299.

Holmes has examined a number of samples of cannabis of varying origin, and finds that the drug from India is more uniformly active.—(Abstr. from Pharm. J., Lond., 1905, v. 20.) Abstr. Pharm. Zentralh., 1905, v. 46, p. 875.

Holmes, E. M., in discussing some recent additions to the museum, reports that Dixon has examined preparations of cannabis made by Umney and finds that the Indian variety is the most active and that the African is a little more active than the French.—Pharm. J., Lond., 1905, v. 21, p. 834.

An abstract (from Bull. Kolon. Mus. Haarlem, 1905, v. 32) calls attention to the use of sirih in the Dutch Indies. The monograph contains a number of prize essays on the subject.—Abstr. Just's Jahresber. (for 1905), v. 33, pt. 3, p. 751.

Moreau, H., has published a monograph "Etude sur le Haschich," Paris, 1904, 8vo., p. 92.—*Ibid.*, p. 751.

Mundy outlines the following specific indications for cannabis indica: Irritation of the urinary organs, with frequent desire to urinate and a burning sensation in the urethra; marked nervous depression with irritability, spasm, or pain, accompanied with neurotic excitement.—Eclectic M. J., 1905, v. 65, pp. 347-349.

CANTHARIS.

The report of the revisors of Vienna pharmacies (Ztsch. d. österr. Apoth. Ver.) asserts that cantharides was found to contain from

3.44 to 14.2 per cent of ash in place of 8 per cent permitted by the Austrian and the German Pharmacopœias.—*Pharm. Prax.*, 1905, v. 4, p. 537.

An abstract points out that cantharides is frequently found to be deteriorated owing to the imperfect drying or lack of care in keeping.—*Südd. Apoth. Ztg.*, 1905, v. 45, p. 758.

Jorissen, A. (from *J. de Pharm. de Liège*), outlines a process for the preparation of cantharidin, by extracting the drug with chloroform after treatment with a mixture of hydrochloric acid and water, evaporating the chloroform solution, washing the residue with petroleum benzine and alkaline water, and finally dissolving the cantharidin in boiling alcohol, filtering and crystalizing.—*Bull. Soc. Roy. de Pharm. de Bruxelles*, 1905, v. 49, p. 7.

Roberts, A. A., discusses the comparative spheres of cantharis, terebinthina, mercurius corr., and plumbum in the treatment of nephritis.—*Tr. Am. Inst. Homœop.*, 1905, v. 61, pp. 368-374.

Coley, T. L. (in *Tran. Coll. Phys., Phila.*, 1905, v. 27, pp. 62-72), contributes an historical sketch on the famous controversy concerning the use of cantharides internally.—Reference from *Ind. Med.*, 1905, p. 1191.

CAPSICUM.

Vanderkleed, Charles E., reports 5 assays of capsicum varying from 9.4 to 23.9 per cent of oleoresin, the standard for a good drug being 15 per cent. All of the samples, except one, assayed over 16 per cent of oleoresin.—*Proc. Penna. Pharm. Ass.*, 1905, p. 55.

Hockauf, J., in the report of the revisors of Vienna pharmacies (from *Ztschr. d. österr. Apoth. Ver.*), mentions a paprika sample containing as much as 4 per cent of a lead salt soluble in acetic acid. The revisors call attention to this report as an indication of the possible contamination that may be found in powdered drugs, either from carelessness or malicious intent.—*Pharm. Prax.*, 1905, v. 4, p. 38.

Lloyd, John Uri, points out that many forms of red pepper pods, both large and small, are sold under the name capsicum. Probably the purchaser of powdered capsicum knows as little concerning the drug that yielded this powdered capsicum as some powderers of drugs care about their composition.—*Pharm. Review*, 1905, v. 23, p. 299.

Harris, J. Arthur, discusses the proliferation of the fruit in capsicum. He concludes, from an extended series of experiments and observations covering a period of years, that proliferation of the fruit, using the term to cover all of the several phenomena, is very common in several varieties of capsicum. It is practically wanting in the slender fruited forms, although some varieties form

exceptions to this rule.—Missouri Bot. Gard., 17th Annual Report, 1906, pp. 130–140.

Francis, John M., believes that he is warranted in asserting that a 94 per cent alcohol is not necessary for the exhaustion of capsicum in the manufacture of the fluid extract. He points out that while capsicum is quite rich in fats these do not contain the active principle desired. He suggests that this oily or fatty matter might be removed and the active portion of the drug exhausted with 70 per cent alcohol (absolute by volume).—Bull. Pharm., Detroit, 1905, v. 19, p. 528.

Gerrard, A. W., makes a contribution to the pharmacy of capsicum. He has conducted a series of experiments to determine the best all-round solvent of the active principles, with a view of obtaining an extract representing the full activity of the drug. He finds alcohol to be a more satisfactory solvent for capsicum than ether, benzine, chloroform, or other organic solvents. The paper includes a formula for two ointments, a capsicum wool and a capsicum plaster, based on the use of a liquid extract of capsicum made by percolating 100 parts of capsicum with 90 per cent alcohol and distilling off the solvent from sufficient of the percolate to have the resulting preparation weigh 50 parts.—Pharm. J. Lond., 1905, v. 21, pp. 153, 168, 196.

Truax, Florence T., in an article on the A B C of eclectic materia medica, designates capsicum as a pure stimulant, oftentimes insidious, diffusible stimulant. In paralysis, paresis, delirium tremens, prostrating diarrhœas . . . In postpartum hæmorrhage, nothing more prompt. In ulceration of the stomach . . . Locally in chilblains.—Eclectic Med. J., 1905, v. 65, p. 538.

CARBONEI DISULPHIDUM.

An abstract from a German patent application figures and describes a modification in the patent granted to E. R. Taylor, of Penn Yan, N. Y., for an electrical oven or furnace for the production of carbon disulphide.—Chem. Ztg. Cöthen, 1905, v. 29, p. 1131.

Pappe, C., reports the spontaneous ignition of carbon disulphide which was being transferred from a glass bottle through a metal funnel to a large glass carboy. The origin of the combustion is ascribed to electric friction, and the author concludes that glass funnels would be safer. (From Pharm. Ztg., 1905, v. 50.)—Proc. Am. Pharm. Ass., 1905, v. 53, p. 720.

Harmsen, Ernst (Vrtljhrschr. f. ger. Med., 1905, p. 422), has demonstrated that carbon disulphide is a blood poison in that it reduces the blood corpuscles, the hæmoglobin, and the leucocytes.—Apoth. Ztg., Berlin, 1905, v. 20, p. 834.

CARDAMOMUM.

Spaeth, E., points out that the amount of mineral matter in cardamom seeds varies materially, and that too much stress should not be placed on the ash content. A minimum requirement for the essential oil is considered desirable. He also points out that commercially satisfactory ground cardamom should consist only of the ground seed, and for this reason the microscopic characteristics of the hulls should be adequately described. The minimum content of essential oil is suggested as 3 per cent. Powdered whole fruit should be declared as such. The maximum ash content of the seed should not exceed 10 per cent, and the amount insoluble in 10 per cent hydrochloric acid should not exceed 4 per cent. The ash content of the whole fruit should not exceed 14 per cent, and the amount insoluble in 10 per cent hydrochloric acid should not exceed 4 per cent.—Ztschr. f. Unters. d. Nahr. u. Genussm., 1905, v. 10, p. 25.

An abstract from the report by Hein. Haensel, in Pirna, reports the study of a variety of cardamom sent from West Africa, said to be the fruit of *Ammomum korarina* di Pareira, which on distillation yielded 1.72 per cent of a volatile oil.—Pharm. Ztg., Berlin, 1905, v. 50, p. 929.

Just's Botanischer Jahresbericht (for 1905), v. 33, part 3, p. 752, contains several references to the cultivation of cardamom and the preparation of the drug for market.

CARBO LIGNI.

Lloyd, John Uri: "The intent is to use the charcoal made from the willow, freshly burned, and finely powdered, but the fact is, few who handle powdered willow charcoal know whether it is obtained from the willow, the beech, or some other tree. Nor do they know whether it has been exposed to the action of the air and absorbed therefrom a load of gas products that may be carried into a remedy."—Pharm. Review, 1905, v. 23, p. 299.

CARUM.

Eberle, E. G., mentions caraway as being one of the medicinal plants now found or grown in Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Spaeth, E., points out that extracted seeds are to be classed among the more common adulterants of caraway, and he therefore believes that the microscopic characteristics of the fruit should be added to an official description, as powdered caraway is frequently sold. Commercially satisfactory caraway should be required to consist of the undamaged seed of caraway that has not been deprived, either

in whole or in part, of its essential oil, and has a strong characteristic odor and taste. The maximum amount of ash, for the air dry drug, should not exceed 8 per cent, and the amount insoluble in 10 per cent hydrochloric acid should not exceed 2 per cent.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, 1905, v. 10, p. 25.

CARYOPHYLLUS.

LaWall, Charles H., reports finding ground clove containing wheat starch.—*Proc. Am. Pharm. Ass.*, v. 53, 1905, p. 18.

Gadd, H. Wippell, points out that the admixture of exhausted flower buds is easily detected by fixing the clove, head downward, on the point of a drawing pin and applying a match to the stalk. Good specimens burn readily.—*Pharm. J., Lond.*, 1905, v. 21, p. 902.

Spaeth, E., points out that among the more common adulterants of this drug are cloves deprived of their oil, clove stems, and cacao shells. The total absence of starch should not be insisted on, but the starch present should be defined as that of the mother clove, which is occasionally present. The starch of ginger should not be present. Commercially satisfactory cloves should be undamaged and consist of the complete flower buds that have not been deprived, either in whole or in part, of their essential oil, and have a strong odor and taste of eugenol. Powdered cloves should be brown-red or brown in color and should possess a strong characteristic odor and taste. The presence of clove stems should not exceed 10 per cent and the amount of essential oil present should be at least 10 per cent. The total ash should not exceed 8 per cent and the amount insoluble in 10 per cent hydrochloric acid should not exceed 1 per cent.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, 1905, v. 10, p. 22.

Herzog, J., presents a preliminary publication on caryophyllin.—*Ber. d. pharm. Gesellsch., Berlin*, 1905, v. 15, p. 121.

Meyer and Honigschmidt (*Monatsh.*, 1905, v. 26, pp. 379-389) discuss the source and character of caryophyllin.—*J. Chem. Soc., Lond.*, 1905, v. 88, Pt. II, p. 456.

CATAPLASMA KAOLINI.

Schimpf, Henry W., in discussing the cataplasm of kaolin, says:

This is similar to certain proprietary clay preparations. It is undoubtedly a very useful preparation and not an entirely novel one, for the peasants of central Europe have long employed a mixture of clay and glycerin as a household remedy for many ailments, especially where poultices were indicated.—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 516.

An editorial expresses the view that—

the introduction of this article comes as a surprise, as the use of these clay poultices has occasioned much criticism and is by some considered as a distinct

retrograde step in modern therapeutics. The ancient cow-dung poultice had almost as much to commend it as this modern prototype. The commercial kaolin which constitutes the basis of this compound makes a nasty, dirty looking mass, and the official product might have had more glycerin added with advantage. It is too stiff.—*Drug Topics*, 1905, v. 20, p. 197.

Francis, John M., says:

While this addition to the pharmacopœia has been severely criticised there can be no gainsaying the fact that the kaolin poultice is very popular, and justly so, as it is permanent, convenient, and, more important still, effective.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 363.

Roth, A. H., records an experimental and clinical study of clay mixture poultices.—*J. Am. M. Ass.*, 1905, v. 44, pp. 1185-1187.

CASSIA FISTULA.

Lyons, A. B., points out that *Cassia fistula* is described in the U. S. P., VIII, as the fruit of the tree producing it, while the dose given is that of *pulp*, and should be so stated.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

CERA.

Francis, John M., points out that beeswax, both white and yellow, is an uncertain quantity as it appears in commerce. During the past three years he has rejected about 20 per cent of the samples submitted because they were grossly sophisticated. Ceresin seems to be the favorite adulterant, and some specimens have even contained water and soluble coloring matter. The tests given in the new pharmacopœia, he believes, are sufficient to protect the buyer.—*Bull. Pharm.*, Detroit, 1905, p. 363.

Vanderkleed, Charles E., examined 6 samples of white wax, of which 2 were pure, 3 contained some paraffin, and 1 contained much paraffin. He also asserts that nearly all the yellow waxes on the market contain paraffin, the amount of this adulterant usually varying with the price. Of many samples examined 2 contained at least 85 per cent and one more than 90 per cent of paraffin.—*Proc. Penna. Pharm. Ass.*, 1905, p. 55.

Havenhill, L. D., presents tabulated results of examinations of wax made in the pharmaceutical laboratories of the University of Kansas.—*Proc. Kansas Pharm. Ass.*, 1905, pp. 89-90.

Wetterstroem, Theo D., points out that yellow beeswax can be found containing from 10 to 15 per cent of ceresin or unsaponifiable paraffin. White beeswax, No. 1, was found to be similarly adulterated, while white beeswax, No. 2, was found to contain not a trace of beeswax.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 313. See also *Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 183, for additional figures.

CERATUM.

An editorial on the U. S. P., VIII, deprecates the addition of petroleum products to the formulas for cerates as being a change of doubtful value. Of the Compound Rosin Cerate the writer says:

A resurrection of the old Deshler's salve, official in the 1870 pharmacopœia, which might have been allowed to rest in peace. It is hardly a fit representative of twentieth-century pharmacy.—Drug Topics, 1905, v. 20, p. 196.

CERII OXALAS.

Wolff, Hermann, discusses the preparation of pure cerium salts, particularly of the double salts with ammonium.—Ztschr. f. anorgan. Chem., 1905, v. 45, pp. 89–115.

Meyer, R. J., presents a chronological list of the publications relating to the rare earths, cerium, ytterbium and thorium, from 1751 to 1905.—Ztschr. f. anorgan. Chem., 1905, v. 45, pp. 416–480.

An unsigned note discusses the work of P. Hollande, who finds that the cerium salts are toxic, the ceric more so than the cerous. As to the symptoms, he finds that there is a striking analogy between cerium and lead. Cerium should be placed among the neuro-muscular poisons.—Sc. Am. Suppl., 1905, v. 59, p. 24588.

CETACEUM.

Francis, John M., points out that in the final test it is better to add the shavings of spermaceti to a few cubic centimeters of aqua ammonia, heat until the former is melted, shake well, cool, and filter—the filtrate is then acidified as indicated.—Bull. Pharm., Detroit, 1905, v. 19, p. 364.

Fendler (Chem. Ztg., v. 29, p. 555) presents some interesting results from the examination of crude sperm oil of known origin.—Abstr. Pharm. J., Lond., 1905, v. 21, p. 115.

CHARTA SINAPIS.

Gerrard, A. W., criticises the official (Ph. Brit.) formula for charta sinapis, and suggests improvements in manipulation. He also cautions against exposure to light and air in the drying process, otherwise the mustard bleaches and the rubber perishes.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 522 (from Pharm. J., Lond., v. 19, p. 805).

CHIMAPHILA.

Eberle, E. G., mentions *Chimaphila umbellata* as being among the medicinal plants found in Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

CHLORALUM HYDRATUM.

Siedler, P., points out that the Ph. Germ., IV, requires a melting point of 58° C.; his experiments would appear to indicate that hydrated chloral melts at 57° .—Pharm. Post, Wien, 1905, v. 38, p. 568.

Kebler, Lyman F., reports a sample of hydrated chloral which melted at 51° C. and contained chloride and chloral alcoholate.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 183.

Schoorl and van den Berg give some account of investigations made to determine the nature of the decomposition produced in hydrated chloral, under varying conditions, more particularly under the influence of air and light.—Ber. d. pharm. Gesellsch., Berlin, 1905, v. 15, p. 414.

Enklaar, J. E. (from Recuil des Trav. Chim., v. 23, pp. 419-438), presents a study of the action of alkalies on hydrated chloral.—Pharm. Weekbl., 1905, v. 42, pp. 170-174.

Rhode, E. (Centralbl. f. Physiol., 1905, v. 19, pp. 503-504), reports some observations on the toxic action of hydrated chloral on the frog's heart.—Biochem. Centralbl., 1905, v. 4, p. 546.

Rabbagliette (Le Monde Dent., Paris, 1905) discusses the treatment of odontalgia with a 15 per cent solution of hydrated chloral in glycerin.—Dental Cosmos, Phila., 1905, v. 47, p. 1137.

CHLORALFORMAMIDUM.

An editorial, in discussing the additions to the U. S. P., VIII, says of chloralformamidum:

The chemical term for chloralamide. More prescribed on the continent of Europe than in the United States, where its use is decreasing.—Drug Topics, 1905, v. 20, p. 196.

CHLOROFORMUM.

Francis, John M., points out that too much care can not be exercised in procuring chloroform of proper quality, and, more important still, that its peculiarities should be recognized and that adequate precaution be taken to insure that it reach the surgeon's hands in good condition. A sample which conforms to all of the requirements of the pharmacopœia may, he asserts, become unfit for anæsthetic purposes within a month by bad usage.—Bull. Pharm., Detroit, 1905, v. 19, p. 364.

Riedel's Berichte quotes Schmidt as giving the boiling point of chloroform as varying from 59° to 61° and points out that this conforms very closely with the results recorded by Riedel, who finds that the higher requirement of the Ph. Germ., IV, 62° is too high, while the lower 60° is not sufficiently low. For varying barometric pres-

tures, however, the variation is not sufficient and should be changed to read from 58.6 to 62.3° C.—Riedel's Berichte, Berlin, 1905, p. 46.

Schoorl and van den Berg review the present status of our knowledge concerning the changes produced under the influence of light and air and report experiments to determine the more common form and decomposition products.—Ber. d. pharm. Gesellsch., 1905, v. 15, p. 387.

An unsigned article reviews the work done by Biltz, Schacht, Schoorl and van den Berg on the influence of light and air on chloroform and iodoform.—Pharm. Ztg., Berlin, 1905, v. 50, p. 951.

Breteau, P. J., in a French patent application enumerates a number of substances which he proposes to use as preservatives for chloroform and for indicating its decomposition.—J. Soc. Chem. Ind., Lond., v. 24, p. 1254.

Cushing, E. W., discusses the decomposition of chloroform vapor by the flame of illuminating gas and quotes several cases of fatal and of untoward results recorded in the literature.—N. Y. M. J., 1905, v. 81, p. 296. Reference from Ind. Med., 1905, p. 258.

Imbert, L. (from L'Union pharm. 1905), reviews the work done on the decomposition of chloroform vapor. He finds that at red heat chloroform is decomposed into C, HCl, and Cl₂. In the presence of air the carbon is decomposed into carbon monoxide.—Pharm. Ztg., Berlin, 1905, v. 50, p. 673.

Doyon, M. (Compt.-rend. Soc. de biol., Paris, 1905, v. 58, pp. 853–855), discusses the elective toxic effect of chloroform on the liver.—Reference from Ind. Med., 1905, p. 788.

An editorial discusses hepatic toxemia as a late effect of chloroform anæsthesia and calls attention to a communication by Bevan and Favill on acid intoxications and late poisonous effects of anæsthetics, which is printed in the same number of the Journal.—J. Am. M. Ass., 1905, v. 45, p. 794.

CHONDRUS.

An abstract (from Suedd. Apoth. Ztg.) presents some data on the collection and the preparation of carrageen in Brittany.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 10.

CHROMII TRIOXIDUM.

Herting, Otto, discusses the change in title and some of the tests for chromic oxide.—Deut.-Amer. Apoth. Ztg., 1905, v. 10, p. 142.

Schimpf, Henry W., commends the change in name as being more correct.—Am. J. Pharm., Phila., 1905, v. 77, p. 553.

Riesenfeld, E. H., reports a study of the reaction occurring between hydrogen peroxide and chromic acid under varying condi-

tions.—J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 1228 (from Ber. 1905, v. 38, pp. 3558–3586).

CHRYSAROBINUM.

Oesterle, O. A., presents a comparative study on the melting point of chrysophanic acid, as determined by several authors, and the causes for the variations that have been noted.—Arch. d. Pharm., 1905, v. 243, p. 434.

Oesterle, O. A., presents a study of chrysophanic acid and its related compounds.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 502.

CIMICIFUGA.

Lloyd, John Uri, points out that cimicifuga is likely to be contaminated with other species of cohosh or actæa, not as intentional adulterations, however, as others are rarer than the more common black cohosh.—Pharm. Rev., 1905, v. 23, p. 300.

CINCHONA.

Francis, John M., expresses the belief that the ether-soluble standard for cinchona alkaloids is not an improvement over the assay standard hitherto employed for the drug.—Bull. Pharm., Detroit, 1905, v. 19, p. 528.

Dohme finds that the ether-soluble alkaloids in cinchona varied from 5.8 per cent in 1902 to 7.1 per cent in 1901. He also reports finding a variation of total alkaloids in red cinchona from 6.05 per cent in 1903 to 6.85 per cent in 1901.—Apothecary, Boston, 1905, v. 17, p. 942.

Vanderkleed, Charles E., reports three assays varying from 3.42 to 9.0 per cent. He also points out that each lot of cinchona needs a careful assay, as the market is full of the drug assaying less than 5 per cent total alkaloid.—Proc. Penna. Pharm. Ass., 1905, p. 55.

Howard (from Pharm. J.) has analyzed a false calisaya and found 5.14 per cent of quinine, 0.24 per cent of cinchonidine, 0.34 per cent of cinchonine, 0.16 per cent of chinidine, and 0.56 per cent of amorphous alkaloids. The bark resembled that of *C. boliviana* Wed. and of *C. calisaya* var. *morada* Planch. The original plant is evidently closely related to *Cinchona calisaya*.—Pharm. Zentralh., 1905, v. 46, p. 670.

Naylor, W. A. H., discusses Alcock's proposition to use an alcoholic solution of potash in place of the aqueous one prescribed in the Ph. Brit., IV. He points out that, contrary to other observers, the process has usually yielded higher results than the authoritative standard.—Pharm. J., Lond., 1905, v. 21, p. 124.

Fromme, G., points out that the gravimetric determination of the alkaloids in cinchona is the only reliable means for determining the

amount of total alkaloids.—Geschäfts-Bericht von Caesar & Loretz, in Halle a. S., 1905, p. 12.

Caesar and Loretz outline a method of assay for cinchona bark which they propose as a titrimetric estimation controlled by a gravimetric separation of the alkaloid from the resulting mixture.—Geschäfts-Bericht von Caesar & Loretz, in Halle a. S., 1905.

Gadd, Sydney C., points out that the official (Ph. Brit., IV) process requires slight modifications and great attention to details to insure satisfactory results.—Pharm. J., Lond., 1905, v. 21, p. 134.

Overton, Burr M. (Proc. Kentucky Pharm. Ass.), has made a comparison of the U. S. P., Prollius' and Haubensak's process of assay, and prefers the latter because of its simplicity and of the results obtained. He also communicates some information relating to the cultivation of *C. ledgeriana* and *C. succirubra* in Java.—Abstr. Proc. Am. Pharm. Ass., 1905, v. 53, p. 639.

Robertson, Philip Wilfred, outlines a volumetric method for the estimation of cinchona alkaloids by means of their double thiocyanates.—Abstr. Chem. News, Lond., 1905, v. 92, p. 257.

van Leersum, P., presents a microchemical method for the estimation of cinchona barks that depends on the solubility of the liberated alkaloids in benzol and chloroform.—Pharm. Weekbl., 1905, v. 42, p. 432.

Tschirch, A. (Schweiz., Wehnschr. f. Chem. u. Pharm.), finds that in common with cola the reddish coloration of cinchona bark is caused by an enzyme that is readily destroyed by water, even at 80°C., in from fifteen to thirty minutes, though it is able to withstand dry heat for some considerable time.—Pharm. Post., Wien, 1905, v. 38, p. 759.

Zimmerman, Albert, in an illustrated article describes the cultivation of cinchona in Java.—Drug. Circ. & Chem. Gaz., N. Y., v. 49, p. 422.

Deistel (Der Tropenpflanzer, v. 9, pp. 578–580) discusses the cinchona plantations of Southeast Africa.—Bot. Centralbl., 1905, v. 100, p. 239.

Just's Botanischer Jahresbericht (for 1905, v. 33, part 3, p. 777) contains several additional references bearing on the cultivation of cinchona. Tschirch reviews a sketch of the history of cinchona bark by Josef Rompel, S. J., who discusses at some length the importance of cinchona to the human race, the literature of cinchona, the pseudo-literature, and the search for authentic history regarding the introduction of the bark.—Apoth. Ztg., Berlin, 1905, v. 20, p. 667.

van der Wielen, P., discusses the history of the cultivation of cinchona, and includes a bibliography.—Pharm. Weekbl., 1905, v. 42, pp. 137–153, 201–218.

CINCHONIDINÆ SULPHAS.

Francis, John M., points out that the following tests may be of assistance in the differentiation of cinchonidine, cinchonine, and quinine:

Optical rotation.—Cinchonine and its salts are dextro-rotate; quinine and its salts are lævo-rotate; cinchonine and its salts are lævo-rotate.

Melting point.—Cinchonine, about 165° C., and cinchonine sulphate, about 198° C.; quinine (rendered anhydrous by drying at about 125° C.), about 175° C.; quinine sulphate (dried by exposure over H₂SO₄), about 205° C.; cinchonidine, about 202° C.; cinchonidine sulphate, about 205° C.

Solubility in ether.—Cinchonine very insoluble (stated to require from 560 to 719 parts); quinine readily soluble (anhydrous requires 4½ parts, crystalline from 22 to 30 parts); cinchonidine sparingly soluble (about 190 parts).

Fluorescence.—Dissolve in water strongly acidulated with H₂SO₄. Cinchonine not more than a faint fluorescence; quinine, pronounced fluorescence; cinchonidine, not more than a faint fluorescence.

Thalleioquin test (see U. S. P., VIII, under quinine).—Cinchonine, no reaction; quinine, marked reaction; cinchonidine, marked reaction.—Bull. Pharm., Detroit, 1905, v. 19, p. 365.

CINNALDEHYDUM.

Umney and Bennett point out that their experience with cinnamic aldehyde, so far, has not been favorable, as it appears to possess a suspicion of the odor of benzoic aldehyde, which is not present in the natural oil of cassia, and which certainly is a disadvantage.—Pharm. J., Lond., 1905, v. 21, p. 146.

CINNAMOMUM.

Spaeth, E., discusses some of the characteristics of the several varieties of commercial cinnamon, and suggests that a cinnamic aldehyde requirement be provided for. He defines cinnamon as being derived from one or more of the three well characterized varieties of cinnamon, and not extracted in whole or in part. The addition of the wild varieties of cinnamon is not permissible. The amount of ethereal oil should not be less than 1 per cent. The ash content of the air dry drug should not exceed 5 per cent, and the amount of ash not soluble in 10 per cent hydrochloric acid should not exceed 2 per cent.—Ztschr. f. Unters. d. Nahr. u. Genussm., 1905, v. 10, p. 33.

Gadd, H. Wippell, asserts that powdered cinnamon bark should not yield more than 6 per cent of ash.—Pharm. J., Lond., 1905, v. 21, p. 901.

Holmes (from Pharm. J., Lond.) describes the bark of *Cinnamomum pedatatum*, a "wild cinnamon," which, he concludes, might be of value as a source of safrol and linalool.—Pharm. Zentralh., 1905, v. 46, p. 689.

COCA.

Francis, John M., believes that for the present the Java coca leaf should be interdicted for any other purpose than the manufacture of cocaine. He seriously questions the advisability of using the Truxillo leaf for the preparation of galenicals, particularly in view of its lesser content of cocaine and its possible or probable content of isotropyl cocaine.—*Bull. Pharm., Detroit*, 1905, v. 19, p. 449.

Vanderkleed, Charles E., reports 6 assays of coca leaf, varying from 0.446 to 0.725, and concludes that the general quality of the drug is very good.—*Proc. Penna. Pharm. Ass.*, 1905, p. 55.

Greshoff, M., discusses the valuation of Java coca, outlines a method of assay and publishes the findings which confirm the general observation that young leaves contain more than twice the amount of alkaloid that is contained in the older ones.—*Pharm. Weekbl.*, 1905, v. 42, pp. 286–290.

de Jong, A. W. K., outlines a modification of the Keller method, in which the dried and powdered coca leaves are treated with a mixture of ammonia and ice cold ether, using hydrochloric acid for the separation of the alkaloid. The method is said to separate all of the available alkaloids, with the exception of benzoylecgonin.—*Chem. Centralbl.*, 1905, v. 76, p. 1198 (from *Rec. trav. chim. Pays-Bas*, v. 24).

An editorial in commenting on wine of coca says:

The introduction of this product can not be commended either on pharmaceutical, medical, or ethical grounds.—*Drug Topics*, 1905, v. 20, p. 199.

Lyons, A. B., points out that the strength of wine of coca ($6\frac{1}{2}$ per cent) conflicts with the desirable principle of uniformity in the percentage strength of galenical preparations.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 257.

Caldwell, Paul, points out that, fluid extract of coca being quite resinous and red wine containing so little alcohol, more added alcohol should be used in making the wine of coca.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 307.

COCAINA.

Vanderkleed, Charles E., points out that although adulterated cocaine is not common, it is well carefully to examine each lot, not only for intentional adulteration, but also for the presence of the more poisonous coca bases, cinnamyl cocaine and isotropyl cocaine, detected by the permanganate and Maclagan's test, respectively.—*Proc. Penna. Pharm. Ass.*, 1905, p. 54.

Carlson (*Pharm. Zentralh.*, v. 45, p. 69) asserts that the addition of the sulphuric acid to the permanganate test is not necessary, and that its omission really makes the test more delicate.—*Pharm. Prax.*, 1905, v. 4, p. 467.

Reichard (Pharm. Ztg., v. 49, p. 150) reviews several known cocaine reactions and proposes a test with a solution of uranium nitrate (1 per cent), to which a few drops of a concentrated solution of potassium sulphocyanate have been added. This mixture produces, in solutions of cocaine hydrochloride, an intensely yellow precipitate.—Pharm. Prax., 1905, v. 4, p. 308.

Aurelj (Giorn. farm. chim., v. 53, p. 385) reviews the reactions for cocaine and the suggestions that have been made by Schärge, Biel, and Siemssen, and outlines a test for cocaine based on the demonstration of the several components.—Pharm. Prax., 1905, v. 4, p. 308.

Höger, Fritz, discusses the substances that are now being used as substitutes for cocaine, and points out the chemical relationship that exists between them.—Apoth. Ztg., Berlin, 1905, v. 20, p. 886.

Daffour and Ribaut (from Rép. de Pharm.) find that decomposition is likely to occur on heating solutions of cocaine, despite all precautions. The most necessary precaution is to avoid glass having an alkaline reaction.—Pharm. Zentrall., 1905, v. 53, p. 929.

Berry, J. M., reports on experiments made to determine the influence of adrenalin chloride on the absorption of cocaine. He concludes that adrenalin does not protect the body against the toxic dose of cocaine, but appears to enhance its toxic action.—Am. J. M. Sc., Phila., 1905, v. 130, pp. 893–902.

Bruardel, P. (from Ann. d'hyg., Paris, 1905, v. 4, pp. 223–255), discusses poisoning by cocaine.—Reference from Ind. Med., 1905, p. 1052.

COCAINÆ HYDROCHLORIDUM.

Siedler, P., points out that the Ph. Germ., IV, requires a melting point of 183°C. On careful heating cocaine hydrochloride was found to melt at 182°, while rapid heating required as high a temperature as 190° and even more.—Pharm. Post., Wien, 1905, v. 38, p. 568.

Gadd, H. Wippell, commends MacLagan's (the U. S. P., VIII, ammonia) test as being the most satisfactory for the detection of other coca alkaloids.—Pharm. J., Lond., 1905, v. 21, p. 902.

COCCUS.

Francis, John M., points out that cochineal is invariably a filled drug, as the trade would not accept an article which had not been whitened and polished with talc or some similar substance. He has examined many samples which yielded more than 6 per cent of ash.—Bull. Pharm., Detroit, 1905, v. 19, p. 449.

Havenhill, L. D., reports a sample of cochineal which contained 5.8 per cent of moisture and 30.5 per cent of ash.—Proc. Kansas Pharm. Ass., 1905, p. 91.

Patch, E. L., reports 26 to 46 per cent ash. Kebler, Lyman F., reports 39 per cent ash, with tinctorial power one-fifth normal.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 183.

CODEINA.

Francis, John M., points out that it is essential that codeine should be tested for freedom from morphine, and also carefully tested for solubility in water. He asserts that some samples of codeine phosphate are not nearly so soluble in water as they should be for "hypodermics."—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 449.

Caspari, Charles E. (*Apoth. Ztg.*, v. 19, p. 874, and *Proc. Am. Pharm. Ass.*, v. 52, p. 386), outlines a method for the determination of codeine in opium.—*Year Book Pharm.*, Lond., 1905, p. 65.

Dekker, J., discusses the solubility of codeine in water, and suggests that the Ph. Ndl. requirement, 1-80, is too high. He believes that 1-117 to 118 of cold water (15° C.) is more nearly correct.—*Pharm. Weekbl.*, 1905, v. 42, pp. 188-189.

Halle, Walter L., in discussing the relationship of codeine to morphine, outlines the history of the former, and gives some additional data and references relating to its production by the methylating of morphine.—*Chem. Ztg. Cöthen*, 1905, v. 29, p. 1264.

Rodionow, N. D., points out that the unequal behavior of codeine and dionin to ammonia and to Wagner's reagent offers a satisfactory method for differentiating between these two substances.—*Pharm. Ztg. Berlin*, 1905, v. 50, p. 561 (from *Farmazeft*, 1905, p. 102).

Pelz (*Deutsch. Med. Woch.*, No. 22, p. 864) reports a case of codeine mania which, the author believes, controverts the frequently made assertion that there is no such thing as a codeine habit.—*Biochem. Centralbl.*, 1905, v. 4, p. 169.

COLCHICI CORMUS.

Beringer, George M., in speaking of the wine of colchicum root, says:

The reason for its dismissal is not understood. It is extensively used.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 415.

Francis, John M., points out that—

In view of the disparity in alkaloidal content, we question the advisability of retaining the colchicum root. Assays of seventeen consignments of colchicum root averaged 0.35 per cent of colchicine; the highest assayed 0.45 per cent, and the lowest 0.20 per cent, 4 of the 17 consignments assaying below the U. S. P., VIII, standard of 0.35 per cent.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 450.

Vanderkleed, Charles E., reports 9 assays of colchicum root, varying from 0.324 to 0.50 per cent of colchicine. The general quality of this drug he believes to be good.—*Proc. Penna. Pharm. Ass.*, 1905, p. 56.

Francis, John M., points out that the assay of extract of colchicum presents exceptional difficulties because of the solubility of colchicine in either acid, or alkaline, aqueous solutions.—Bull. Pharm., Detroit, 1905, v. 19, p. 494.

COLCHICI SEMEN.

Francis, John M., examined 11 samples of colchicum seed, representing about 60,000 pounds, which assayed an average content of 0.60 per cent of colchicine; the highest was 0.90 per cent and the lowest 0.50 per cent; four out of the eleven samples assayed below the U. S. P., VIII, standard of 0.55 per cent [later 0.45] of colchicine.—Bull. Pharm., Detroit, 1905, v. 19, p. 450.

Dohme, A. R. L., found colchicum seed to vary from 0.60 per cent in 1904 to 0.53 per cent in 1905.—Apothecary, Boston, 1905, v. 17, p. 942.

Vanderkleed, Charles E., reports two assays, 0.30 and 0.462 per cent. He believes the general quality of the drug to be poor.—Proc. Penna., Pharm. Ass., 1905, p. 56.

COLCHICINA.

Francis, John M., thinks it essential that colchicine should be yellow and not brownish, and that it should be readily soluble in water and chloroform. He asserts that much of the commercial colchicine is quite impure, and reports rejecting three consignments which contained only 66.7, 63.6, and 63 per cent, respectively, of pure colchicine.—Bull. Pharm., Detroit, 1905, v. 19, p. 450.

Lyons, A. B., points out that the dose given is only 0.0005 gm., while the dose of colchicum seed is 0.20 gm.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 261.

Dearborn, F. M., discusses the use of colchicine in the treatment of skin diseases.—Tr. Am. Inst. Homœop., 1905, v. 61, pp. 416–418.

COLLODIUM.

Eberle, E. G., recommends that the pharmacopœial method be reversed, so that the alcohol is added first; allow to stand until the pyroxylon is thoroughly saturated, then add the ether and shake.—Apothecary, Boston, 1905, v. 17, p. 951.

Francis, John M., points out that collodions have been made very popular of late years under proprietary names, and that celluloid and acetone are being used to replace the official substances.—Bull. Pharm., Detroit, 1905, v. 19, p. 450.

Lorenzen (Pharm. Ztg., 1905, v. 50, p. 20) notes that the turpentine directed in the Ph. Germ., IV, may be a source of possible impurity

in flexible collodion, and recommends that this substance be dissolved and filtered before being added.—Abstr. in Proc. Am. Pharm. Ass., 1905, v. 53, p. 523.

COLOCYNTH.

Lyons, A. B., points out that the U. S. P., VIII, describes the peeled fruit, but that the dose given is that of the drug *deprived of seeds*.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 261.

Francis, John M., notes that there are few drugs which offer greater temptations to fraud than this. The U. S. P. requires that from 60 to 75 per cent of the weight of the drug must be sacrificed by discarding the seed and the rind. Besides this loss, there must be added the labor involved, and it naturally follows that there is a strong temptation to grind all together and extract in the usual way.—Bull. Pharm., Detroit, 1905, v. 19, p. 450.

Lloyd, John Uri, points out that colocynth may be true to name, of prime fresh quality, and yet not in a condition to be used in medicine. The loss in the required manipulation is so great that some persons can not bear to meet the issue.—Pharm. Review, 1905, v. 23, p. 300.

Howard, Clarence, in recording twenty years' experience with colocynthis, says:

Neuralgic attacks in any part of the body, following the wounding of pride, anger, a display of ungovernable temper, are quickly relieved by colocynthis.—Hahneman. Month., Phila., 1905, v. 40, p. 791.

CONIUM.

Vanderkleed, Charles E., reports 3 assays of conium seed varying from 0.40 to 0.76 per cent of coniine.—Proc. Penna. Pharm. Ass., 1905, p. 56.

Rusby, H. H., believes that conium preparations are considered to be unreliable by physicians largely because the quality of the drug is poor.—Merck's Rep., N. Y., 1905, v. 14, p. 212.

Naylor, W. A. H., points out that, from the experiments of Findlay, coniine may be regarded as the active principle of conium, the other alkaloids not existing in large enough proportions to greatly modify its action.—Pharm. J., Lond., 1905, v. 21, p. 126.

Maben, Thomas, believes that standards should be based on the commercially obtainable drug of fair quality, and points out that the inferior quality of commercial conium may be due to the fact that it is much easier to harvest the ripe than the unripe fruit.—*Ibid.*, p. 140.

v. Braun, J., reports some experiments made to separate the several alkaloidal bases present in conium.—Ber. d. deutsch. chem. Gesellsch., 1905, v. 38, pp. 3108-3112.

Tunmann, D., reports that out of 10 samples of (German) hemlock herb only 6 were free from adulteration. He recommends the deletion of the herb from the Ph. Germ.—Pharm. Zentralh., 1905, v. 46, p. 879.

COPAIBA.

Francis, John M., has met with many samples of copaiba that fell below the minimum limit of specific gravity (0.950). Of 19 samples examined, 8 ranged in specific gravity from 0.938 to 0.924. He believes that the American trade favors a light-colored copaiba, and this he asserts is synonymous with low specific gravity. The U. S. P., VIII, test for gurjun balsam he believes to be too delicate, and hence unreliable. He also points out that the condensation of copaiba balsam develops some constituent which responds to the test for gurjun balsam.—Bull. Pharm., Detroit, 1905, v. 19, p. 450.

Caeser and Loretz suggest the limitations of specific gravity at 15° C. as being between 0.970 and 0.990. They believe the ammonia test to be a more reliable indication of the purity of copaiba than the determination of the saponification and acid numbers, and that the latter is useless unless it has been shown that both resin and gurjun balsam are absent.—Geschäfts-Bericht von Caeser & Loretz, in Halle, a. S., 1905, p. 76.

Vanderkleed, Charles E., reports 1 out of 6 samples examined as being adulterated.—Proc. Penna. Pharm. Ass., 1905, p. 54.

Wetterstroem, T., reports 5 samples examined—one U. S. P. Three contained gurjun balsam and one was fictitious.

Gane reports an unusually high proportion of volatile oil (84 per cent).—Proc. Am. Pharm. Ass., 1905, v. 53, p. 184.

The inspectors of pharmacies in Belgium found copaiba adulterated with fatty oils and gurjun balsam.—Bull. Soc. Roy. de Pharm. de Bruxelles, 1905, v. 49, p. 307.

Schimmel & Co. report on the examination of Para, Bahia, and Angostura copaiba.—Schimmel & Co. Semi-Ann. Rep., 1905, April-May, pp. 24-26.

Kline, C. M., discusses the introduction of African balsam, its use as an adulterant and its possible use as a medicinal agent. He concludes that African copaiba is the product of a genuine copaiba, closely related to the South American variety, and that there is clinical proof to support the assertion that when sold under its own name it should be granted a legitimate position in the materia medica.—Am. J. Pharm., Phila., 1905, v. 77, pp. 185-188.

Schimmel & Co. publish an abstract (from J. de la Parfum et Sav. Franc., 1905, v. 18) which contains some account of the production of gurjun balsam, its origin and its uses.—Schimmel & Co. Semi-Ann. Rep., 1905, April-May, p. 48-49.

CONVALLARIA.

Gienapp, E. (Wiener illustr. Gartenztg., 1905, pp. 66-70), presents an article on the cultivation of convallaria, the exportation of the plant to America, and the preservation of the young plants by means of ice.—Bot. Centralbl. for 1905, v. 100, p. 91.

CORIANDRUM.

Eberle, E. G., mentions coriander among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Spaeth, E., points out that commercially satisfactory coriander should not yield more than 7 per cent of ash and that the portion insoluble in 10 per cent hydrochloric acid should not exceed 2 per cent.—Ztschr. f. Unters. d. Nahr. u. Genussmittel, Berlin, 1905, v. 10, p. 25.

CREOSOTUM.

Francis, John M., points out that the tests for phenol and coal-tar creasote are ample; the coeruleignol test is very important and the one most likely to be needed.—Bull. Pharm., Detroit, 1905, v. 19, p. 450.

CRESOL.

An editorial note on cresol asserts that it is "difficult to obtain, of good quality, in this market."—Drug Topics, 1905, v. 20, p. 196.

The same assertion is contained in correspondence to H. J. Eberle.—Am. Druggist, 1905, v. 47, p. 297.

The Ph. Hisp., VII, requires that cresol have a specific gravity of approximately 1.045; that it boil at from 185 to 205° C., and be soluble in from 40 to 50 parts of water at ordinary temperatures, and freely soluble in strong alcohol, glycerin, or ether.—Farmacopea Oficial Española, 1905, p. 231.

An abstract (from Riedel's Report) outlines a method for the approximate determination of cresols and phenols in crude cresols.—Year Book of Pharmacy, Lond., 1906, p. 29.

Hallberg, C. S. N., discusses cresol and its solution. The article is accompanied by some additional comments brought out in discussion.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 417-419.

Adam, Paul, presents a comparative study of several formulas that have been proposed or are included in other pharmacopœias. He proposes a simple mixture of equal parts of cresol and 30 per cent solution of sodium hydrate.—J. de pharm. et de chim., Paris, 1905, v. 22, p. 145.

Tollens, Karl, reports a comparative study of the toxicity of cresol and the saponaceous preparations of cresol with similar preparations of phenol. The experiments lead him to conclude that a cresol soap

solution is at least equally as toxic as a corresponding phenol soap solution or a simple solution of phenol of equal strength.—Arch. f. exper. Path. u. Pharmacol., Leipz., 1905, v. 52, pp. 220-241.

Kochmann, Martin, reports a series of experiments on the toxicity of lysol (a cresol soap solution), undertaken because of the great frequency of lysol poisoning in Germany. Includes a comprehensive review of the literature.—Arch. internat. de Pharmacod. et de Thérap. 1905, v. 14, pp. 402-428.

CRETA PRÆPARATA.

Williams, John K., points out that the presence of sugar in compound chalk powder causes the resulting mixture to sour readily; the glycerin of a former pharmacopœia should never have been left out. He suggests a formula using sugar of milk and saccharin.—Proc. Connecticut Pharm. Ass., 1905, p. 49.

CUBEBA.

Sage, C. E., describes a false cubeb that has appeared on the London market in appreciable quantity. The fruit is smooth, of a brownish color, and has little or no oil. It is probably derived from *Piper ribesoides* Wall., described by de Wevre.—Chem. & Drug., Lond., 1905, v. 67, p. 797.

CUPRI SULPHAS.

Crouzel (Ann. de chim. analyt., Paris, v. 9, p. 422) discusses the detection of ferrous sulphate in cupric sulphate.—Year Book of Pharm., Lond., 1905, p. 70.

Spannbauer records a case of poisoning by the external application of a solution of copper sulphate in milk, as a remedy for eczema.—Nouv. Rem., 1905, v. 21, p. 451.

Fuller, Geo. W., reviews the uses of copper sulphate as a germicide in connection with the purification of water.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 1059.

CYPRIPEDIUM.

House, Homer Doliver, contributes some notes on the orchids of central New York, and concludes that we have three species of yellow lady's slipper, one large, and one small flowered, both with vertically flattened lip, and a third one with laterally flattened lip.—Bull. Torrey Bot. Club, N. Y., 1905, v. 32, p. 374.

DECOCTA.

The Spanish Pharmacopœia contains fifteen formulas for decoctions, six of them compound.

Björzell, Otto, discusses the directions for preparing the decoctions of the Swedish Pharmacopœia.—Svensk. Farm. Tidskr., 1905, v. 9, pp. 8-10.

Sjöberg, Knut, discusses the communication by Björzell.—*Ibid.*, pp. 35-37.

DIGITALIS.

The Bureau of Plant Industry reports the successful cultivation of digitalis at Washington, but points out that since the plant occupies the soil for two years and yields only the leaves at flowering time the outlook for good financial returns is hardly as favorable as in the case of belladonna, for instance.—Ann. Rep. Dept. Agriculture, 1905, p. 148.

Jenner, Edmund F. L., reports observations in connection with two plants of digitalis. One grown on stable manure was upwards of 8 feet high and had leaves fully a foot long; the other, on ordinary soil, was not more than 15 inches high and had leaves not more than 3 inches long.—Canad. Druggist, 1905, v. 17, p. 406.

Francis, John M., points out that the revisers of the U. S. P. might well have included the warning that this drug deteriorates badly with age.—Bull. Pharm., Detroit, 1905, v. 19, p. 451.

Collin, Eug., reviews the history, uses, and pharmacognosy of digitalis. The article is illustrated with two figures, showing the structural characteristics as seen in powdered digitalis and the structures of some of the more frequently found adulterants, such as *Inula conyza*, *Verbascum phlomoïfes*, *Artanthe elongata*, and *Salvia sclarea*.—J. de pharm. et de chim., Paris, 1905, v. 22, p. 56.

Caeser and Loretz point out that the characteristic structures of digitalis, in the finely ground drug, offer some difficulty in recognition; this is not apparent in the coarse powder or the granulated drug. They also point out that the leaves of digitalis collected during the months of July and August are more uniformly reliable and active than are leaves that are collected earlier in the year. They also assert that the adulteration of digitalis, apart from the accidental admixture of grass, is a matter of rare occurrence and that the recently reported cases of sophistication with *Verbascum* are no doubt due to careless mistaking of one drug for another.—Geschäfts-Ber. von Caeser & Loretz, in Halle a. S., 1905, pp. 28-31.

Dohme, A. R. L., has found that digitalis runs rather uniform in digitoxin strength. During seven years, 1899 to 1905, inclusive, the lowest was 0.23 per cent, found in 1903, and the highest 0.30 per cent in 1904 and 1905.—Apothecary, Boston, 1905, v. 17, p. 942.

Mitlacher, W. (Pharm. Post, Wien, 1905, p. 41), reports finding *Inula conyza* leaves in digitalis, and calls attention to the charac-

teristic structure of the hairs.—Abstr. Am. Druggist, 1905, v. 47, p. 238.

Moeller, J. (Pharm. Post, v. 37), reports finding *Verbascum* leaves in place of digitalis.—Pharm. Prax., 1905, v. 4, p. 109.

The revisors of Vienna Pharmacies (Ztschr. d. Oesterr. Apoth. Ver.) report finding digitalis leaves containing as high as 29.4 per cent of ash, while other figures varied from 7.5 to 12.85 per cent. They say:

So high an ash content in a drug that is of such great importance is not at all permissible, and the pharmacist's attention should be directed to the fact that leaf drugs containing hairs are particularly prone to contain sand, dirt, and dust and should be tested for ash.—Pharm. Prax., 1905, v. 4, p. 37.

Kiliani, H., reports a comparative study of the several digitonins prepared by Schmiedeberg, Cloetta, and Kiliani. He outlines a method for preparing the amorphous digitonin and concludes that Cloetta's "amorphous digitonin" is certainly a mixture, and is not properly represented by so simple a formula as $C_{28}H_{47}O_{14}$.—Arch. d. Pharm., 1905, v. 243, p. 5-12.

Focke, C. (from Med. Klin., 1905, p. 775), recommends the use of uniformly active preparations of digitalis, preferably an infusion, not older than two days, made from an assayed leaf. He also points out that digitoxin does not fully represent the action of digitalis.—Apoth. Ztg., Berlin, 1905, v. 20, p. 586.

An editorial reviews the controversy as to whether infusion of digitalis should be filtered, and concludes that in consideration of the several points that have been made it would appear to be preferable to direct that infusion of digitalis be directed to be shaken, in preference to being filtered.—Deut.-Amer. Apoth. Ztg., 1905, v. 26, p. 91.

Kakowski (from Arch. internat. de Pharmacodyn, v. 15, pp. 21-139) discusses the action of several digitalis preparations on the heart and compares this typical heart action with the action of barium chloride, adonidin, coronillin, helleborin, pyramidon, and a number of other substances.—Biochem. Centralbl., 1905, v. 4, p. 445.

Plumier, L. (J. de Physiol. et Pathol. Generale, 1905) reports on a series of experiments relating to the action of digitoxin, digitalin, and alcohol on the cardio-pulmonary circulation.—Biochem. Centralbl., 1905, v. 4, p. 167.

Korezki, A. (from Russky Wratch, 1905, p. 746), has studied the local anæsthetic action of substances belonging to the digitalis group, particularly solutions of strophanthin, digitalin, adonidin, and helleborin; their action on the conjunctiva of the rabbit and on the skin and the nerves of the frog. He concludes that while the local anæsthetic action is more slowly induced it is more prolonged than with cocaine. Adonidin and helleborin are more promising than strophan-

tin and digitalin. Adonidin, on account of its lesser degree of toxicity, is to be preferred.—Pharm. Ztg., Berlin, 1905, v. 50, p. 921.

Baker, W. F., asserts that the toxic effects of digitalis, delirium and hallucinations, developed in the course of treatment of cardiac cases with digitalis, rapidly disappear on withdrawing the medicine.—Hahneman, Month., Phila., 1905, v. 40, p. 796.

ELASTICA.

Fendler, G., discusses the several methods suggested for the examination of crude rubber, and reports his results.—Arb. a. d. Pharm. Inst. d. Univer., Berlin, 1905, v. 2, pp. 278-305.

Fendler, G., discusses the solubility of various kinds of crude rubber in ether, benzin, and benzole, and of a lesser number of samples also in chloroform and carbon disulphide. He presents a table giving a review of the behavior of the several kinds of rubber examined.—*Ibid.*, pp. 306-317.

Ule, E. (Engl. Jahrb., 1905, v. 35, pp. 663-668), discusses the origin of the rubber obtained on the Amazon River, enumerates the plants yielding it, and discusses their distribution.—Abstr. in Bot. Centralbl., 1905, v. 99, pp. 129.

Additional references on the origin and on the cultivation and production of "Elastica" will be found in *Ibid.*, 1905, v. 100, pp. 63, 144, 252, and 255.

Just's Botanischer Jahresbericht (for 1905, v. 33, pt. 3, pp. 789-815) contains a number of additional references on "Elastica" indicative of the widespread interest that is being manifested in this particular product.

ELATERINUM.

Francis, John M., points out that this product varies greatly in effectiveness, and that there is only one way to insure its quality—try it on yourself or your friends.—Bull. Pharm., Detroit, 1905, v. 19, p. 451.

ELIXIR ADJUVANS.

An editorial says:

The new elixir adjuvans makes a fairly palatable liquid, but we should have preferred to see the old N. F. Elixir Adjuvans introduced without change, as the latter served admirably the purpose for which it was designed.—Drug Topics, 1905, v. 20, p. 196.

ELIXIR FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM.

Francis, John M., asserts that he is not prepared to say that the formula given in the new pharmacopœia is not a success, but is inclined to be skeptical until time has proven that the problem is successfully solved.—Bull. Pharm., Detroit, 1905, v. 19, p. 451.

An editorial expresses the belief that the official instructions for manufacturing this elixir are unnecessarily complicated.—*Drug Topics*, 1905, v. 20, p. 196.

Lyons, A. B., expresses the belief that an assay process should be given, since comparatively few druggists will make the elixir themselves, particularly by a formula so troublesome.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

EMPLASTRUM PLUMBI.

Francis, John M., asserts that there is really no reason why the soap should be dried, powdered, and then dissolved in water except that it enables one to use exact proportions and thus avoid possible waste. He believes that it will be equally economical and more satisfactory if the bar of castile soap is dissolved in water so as to produce a thin solution, lead acetate in solution then being added so long as a precipitate forms; as soon as this point is reached all of the soap is consumed and the operation can be carried out as directed by the pharmacopœia.—*Bull. Pharm.*, Detroit, 1905, v. 19, pp. 452.

An editorial expresses the fear that some difficulty will be experienced in freeing the plaster from water when operating on a small scale.—*Drug Topics*, 1905, v. 20, p. 197.

EMULSA.

Williams, John R., recommends the so-called continental or "dry" method for making emulsions, and prefers the use of a perfectly dry mortar in place of a bottle. In making emulsions of essential oils he proposes the addition of from 10 to 15 per cent of "expressed oil."—*Proc. Connecticut Pharm. Ass.*, 1905, p. 52.

Francis, John M., points out that only the best grades of tragacanth and of acacia are suitable for emulsions. He believes that the pharmacist who has had difficulties with emulsions will see them disappear when he improves the quality of his emulsifier.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 452.

Kebler and Hoover outline a scheme for the analysis of emulsions, and present the results of their own experiments in tabular form.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 354-364.

The Spanish Pharmacopœia contains formulas for six emulsions, including: *Emulsio camphorata*, *emulsio arabica*, *emulsio communis*, *emulsio olei jecoris aselli*, *emulsio olei jecoris aselli hypophosphitici*, *emulsio gummi-resinæ ammoniaci*.

EMULSUM OLEI MORRHUÆ.

Francis, John M., points out that there may be some doubt as to the practicability of the U. S. P. formula for emulsion of cod-liver

oil with hypophosphites, and advises against the making up of any considerable amount of stock until the pharmacist has proven the process and gained the necessary skill through actual trial.—Bull. Pharm., Detroit, 1905, v. 19, p. 452.

EPINEPHRINA.

Aldrich, Thos. B., reviews the history of the active principle of the suprarenal glands from Addison (1855) to Takamine (1901) and discusses the empirical and structural formulas. He also presents an extensive bibliography bearing more directly on this particular phase of the work.—J. Am. Chem. Soc., 1905, v. 27, pp. 1074–1091.

Abel and Taveau discuss the differences that occur in the nitrogen content of epinephrin prepared at different times, and the changes produced by repeated solution and precipitation. They point out that the generally accepted constitutional formula for epinephrin does not correspond to all of the facts brought out by a study of the decomposition products, and should not be accepted without further investigation.—J. Biol. Chem., N. Y., 1905, v. 1, pp. 1–32.

Bertrand, Gabriel (Bull. Soc. Chim., v. 31, pp. 1289–1292), records the physical characteristics of adrenalin.—Analyst, London, 1905, v. 30, p. 22.

Abelous, Soulié, and Toujan (Compt.-rend. soc. biol., v. 58, pp. 301–302, 533–534, 574–576) discuss a colorimetric determination of adrenalin by means of iodine, the formation of adrenalin by the adrenal gland, and the origin of adrenalin.—Abstr. in Jahresb. (for 1905), ü d. Tier-Chemie, 1906, v. 35, p. 564.

Kwisda, A., discusses the reports on the blood pressure raising principle of the adrenal gland, published during the past few months by French and German investigators.—Schweiz. Wchnschr. f. Chem. u. Pharm., 1905, v. 43, p. 351.

Friedmann, E., has attempted to solve the question regarding the constitution of adrenalin by synthesis, from the substance described by Fürth as tribenzolsulfoadrenalin. Friedmann agrees with Jowett as regards the structural formula for adrenalin.—Beitr. z. chem. Phys. u. Path., 1905, v. 6, p. 93.

Barger and Jowett present a discussion of the synthesis of substances allied to epinephrin, and present experimental data relating to the production of these substances.—J. Chem. Soc., Lond., 1905, v. 97, part 2, pp. 967–974.

Dakin, Henry Drysdale, discusses the synthesis of substances allied to adrenalin and gives a detailed account of a compound having the constitution generally accepted for adrenalin.—Biochem. Centralbl., 1905–6, p. 567. See also Proc. Roy. Soc., Lond., v. 76, pp. 491–497; and for a discussion of the physiological activity of substances indirectly related to adrenalin; *Ibid.*, pp. 498–503.

Stolz, Friedrich (Ber., v. 37, pp. 4149-4254), discusses adrenalin and alkylaminoacetylcatechol. reports results identical with those of Jowett. and suggests the possibility of a synthesis of the base by reducing methylaminoacetylcatechol.—Abstr. in J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 106.

Ehrmann, R., presents a comparative test for adrenalin which depends on the method outlined by Meltzer and Auer (Am. J. Physiol., 1904, v. 11, p. 449) of determining the action of this substance on the enucleated eye of a frog.—Arch. f. expt. Path. u. Pharmacol., 1905, v. 53, pp. 97-111.

Ehrmann, Rud., discusses the work done by Langley (J. Physiol., v. 27, p. 237) and concludes that adrenalin produces a marked increase in the secretion of the cutaneous glands of the frog. Atropine, it was found, did not control this increased action, as the atropine itself was rapidly eliminated in this way.—*Ibid.*, pp. 137-139.

De Vos and Kochmann report a series of experiments made to determine the rapidity with which the active principle of the suprarenal capsule is absorbed or destroyed when injected intravenously.—Arch. internat. de Pharmacol. et de Thérap., 1905, v. 14, pp. 81-91.

Loewi, O., discusses the action of synthetic, adrenalin-like, products, and the probable constitution of adrenalin.—Arch. f. expt. Path. u. Pharmacol., 1905, v. 53, pp. 213-226.

Benedicenti, A. (Giornale d. R. Acad. di Med. di Torino, v. 48, pp. 553-571), records his observations of the action of adrenalin on the pancreas secretion in dogs.—Abstr. in Jahresb. (for 1905) ü. d. Tier-Chemie, Wiesbaden, 1906, v. 35, pp. 485-487.

Loeb and Githens report a series of experiments made to determine the effect of experimental or abnormal conditions on the effect produced by adrenalin. Among the conditions studied were: Influence of thyroidectomy, influence of renal lesions, influence of pregnancy, and the relation of certain other lesions.—Am. J. M. Sc., 1905, v. 130, pp. 658-670.

Möller, S., reports an experimental study of the action of adrenalin the circulation.—Therap. Monatsh., 1905, v. 19, p. 546.

Josué, O. (J. de Physiol. et de Path. gén., v. 7, p. 690), reports a histologic study of the atheromatous conditions of arteries supposedly produced by the use of adrenalin.—Biochem. Centralbl., 1905, v. 4, p. 376.

Foa and Gatin discuss the action of adrenalin on the reaction of the blood.—Compt.-rend. Soc. de Biol. Paris, 1905, v. 75, pp. 145-148.

Bouchart, A. (Rec. d'Ophth., 1905, v. 27, pp. 30-36), discusses accidents attributable to adrenalin and reports an accident with the use of adrenalin in the eye, resulting in a permanent opacity of the cornea, irregular contraction of the pupil, and considerable change in the iris.—Biochem. Centralbl., 1905, v. 4, p. 171.

Wiggers, Carl J., points out that adrenalin acts upon the cerebral vessels, causing constriction in the same manner as on the vessels of other organs, and that the reaction of the cerebral vessels to adrenalin is a trustworthy proof, or at least indicative of the existence of cerebral vaso-constrictor nerves.—*Am. J. Physiol.*, 1905, v. 14, pp. 452-465.

Be Beck, D., reports an accident with adrenalin (*Ann. Ophthal.*, St. Louis, 1905, v. 14, p. 511).—Reference from *Ind. Med.*, 1905, p. 1052.

ERGOTA.

Francis, John M., points out that the one specification that is not accepted at its full importance is that ergot is unfit for use after it is a year old. He asserts that enormous quantities of ergot are sold in the market of the United States, and does not hesitate to declare that a very large proportion of it is worthless, or at least so inferior as to render it unfit for medicinal use. As a logical sequence a considerable proportion of the ergot preparations are also woefully wanting in therapeutic activity. "Ergot is not ergot because it is so labelled."—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 452.

Vanderkleed, Charles E., reports four assays of ergot varying from 0.16 to 0.31 per cent of cornutin, and concludes that the general quality of ergot is good.—*Proc. Penna. Pharm. Ass.*, 1905, p. 56.

Dohme, A. R. L., says:

The per cent of cornutin noted in the laboratory report varied from 0.32 per cent in 1904 to 0.12 per cent in 1905.

He points out that in the latter year it has been almost impossible to secure any ergot that approached the 0.2 per cent standard for cornutin. He also points out that—

Bold ergot is less rich in cornutin than smaller, less bold ergot.—*Apothecary*, Boston, 1905, v. 17, p. 942.

Philip Röder, Wien, reports two ash determinations of ergot which gave 3.18 and 3.24 per cent, respectively, or 3.45 and 3.46 per cent in the water-free substance.—*Pharm. Post*, Wien, 1905, v. 38, p. 391.

The revisors of Vienna Pharmacies report finding one sample of powdered ergot which contained flour as an adulterant.—*Pharm. Prax.*, 1905, v. 4, p. 38.

Caeser and Loretz outline a method for the determination of cornutin in ergot, as follows:

The ergot is percolated with petroleum ether to remove the fat. The resulting drug, after previous drying, is treated with a mixture of ether, magnesia, and water, an aliquot part of the resulting ethereal solution is washed out with 0.5 per cent of hydrochloric acid. The washings are then heated to remove the last traces of ether, made alkaline with ammonia, and then washed with ether; the latter is finally removed by distillation and the resulting dry ma-

terial weighed.—Geschäfts-Bericht von Caesar & Loretz, in Halle a. S., 1905, p. 97.

Vahlen, Ernst (Deutsch. Med. Wchnschr., 1905, p. 1263), reviews the work done by Kobert and Jacobs on the active principle of ergot, and describes a new, water soluble substance which he calls clavin, which he believes more fully represents the desirable medicinal properties of ergot than do any of the other preparations now available.—Apoth. Ztg., Berlin, 1905, v. 20, p. 642.

Schaerges, C., reviews the chemical work that has been done on ergot, enumerates the several substances isolated, and refers particularly to secornin, a trade name for Ergotin Keller.—Pharm. Zentralh., 1905, v. 46, p. 789.

Francis, John M., discusses the use of the official extract of ergot for hypodermic injection, and asserts that this extract contains some principles that are decidedly objectionable for use in this way, in addition to the ever present danger of bacterial infection.—Bull. Pharm., Detroit, 1905, v. 19, p. 494.

Zahner, W. U., points out the possibility of infection or the objectionable nature of the preservatives present in the aqueous solutions of ergot offered for hypodermic injections.—Proc. Texas Phar. Ass., Texas Druggist, 1905, v. 7, p. 21.

Cline, R. R. D., discusses the preservation of drugs like ergot and outlines a method for the preparation of a fluid extract of ergot, which he believes to be preferable to the official process.—*Ibid.*, p. 21.

Sollmann and Brown report a series of experiments on the effects of intravenous injection of ergot on the mammalian circulation.—J. Am. M. Ass., Chicago, 1905, v. 45, pp. 229-240.

Jolly, Philip Carl, has prepared a monograph (Göttingen, 1905, W. F. Kastner, 133 pages, 8vo.) discussing the influence of ergot on the circulation.—Reference from Ind. Med., 1906, p. 66.

Orlow (Neurolog. Westnik, v. 11) discusses the functional disturbances in the eye caused by the poisonous action of ergot.—Biochem. Centralbl., 1905-6, v. 4, p. 593.

Mundy discusses the specific uses and the indications of ergot in eclectic practice.—Eclectic. M. J., 1905, v. 65, pp. 398-400.

ERIODICTYON.

Meyer, Gust., recommends a syrup of eriodictyon as a corrigent for such drugs as quinine, hydrastis, and aspidium.—Pharm. Ztg., Berlin, 1905, v. 50, p. 856.

EUCALYPTOL.

The inspectors of pharmacies, Belgium, found samples of eucalyptol substituted by oil of eucalyptus.—Bull. de la Soc. Roy. de Pharm. de Bruxelles, 1905, v. 49, p. 311.

EUCALYPTUS.

Baker and Smith describe some West Australian eucalypts and their essential oils.—Pharm. J., Lond., 1905, v. 21, p. 382.

Smith, H. G. (communication to Roy. Soc., New South Wales), discusses the presence of calcium oxalate in the barks of the eucalypts.—Abstr. in Pharm. J., Lond., 1905, v. 21, p. 116.

EUGENOL.

Frankforter and Lands present an exhaustive study on eugenol and some of its derivatives. They report that a sample of eugenol bought as pure contained organic impurities, considerable quantities of water, and some inorganic matter. After purification, the boiling point was found to be 244.5° C.; sp. gr., 1.0689 at 20° C.; index of refraction, 1.54437.—J. Am. Chem. Soc., 1905, v. 27, pp. 641–649.

EUONYMUS.

Eberle, E. G., enumerates euonymus among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Lloyd, John Uri, points out that so far as the drug is concerned, wahoo is true to name, but large quantities of the bark of the shrub and twigs, as well as the whole root, are sold in the market. Only the bark of the root is used in eclectic medicine, and that alone should be employed under the name euonymus.—Pharm. Rev., 1905, v. 23, p. 301.

An abstract (from Pharm. J., Lond., 1905) points out that the bark of *Alstonia scholaris* has been met with on the London market as an adulterant of *Euonymus atropurpureus*. As the two marks resemble each other in many respects, Holmes gives a detailed description of them.—Pharm. Zentralh., 1905, v. 46, p. 711.

Bangert, J. R., calls attention to the specific indications for euonymus, and points out that its main action is upon the glandular organs, especially the liver.—Eclectic Med. J., 1905, v. 65, p. 494.

EUPATORIUM.

Eberle, E. G., lists eupatorium among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Robinson, B. L., presents diagnoses and notes relating to American *Eupatoria*, including descriptions of eight new species.—(Proc. Am. Acad. Arts and Sci., v. 41, pp. 271–278.) Bull. Torrey Bot. Club, N. Y., 1905, v. 32, p. 447.

Lloyd, John Uri, asserts that this herb is often substituted for the root of *Eupatorium purpureum* (Queen of the Meadow or Gravel Root), and that the reverse is often true as concerns the latter drug.

This confusion arises because of the confusion of names. Substitution is not through intent, but through ignorance.—*Pharm. Rev.*, 1905, v. 23, p. 301.

Mundy enumerates the several conditions in which eupatorium is indicated.—*Eclectic Med. J.*, 1905, v. 65, p. 572.

EXTRACTUM MALTI.

Woocock, E. C., says of extract of malt:

This preparation, Rip Van Winkle-like, has been allowed to sleep for twenty years, and on awakening has found itself rather antique. The directions to evaporate to the consistence of thick honey, regardless of existence of degrees in specific gravity, are obsolete.—*Am. Druggist*, 1905, v. 47, p. 317.

Francis, John M., suggests that the real demand of the situation has been overlooked because the pharmacopœia gives no means for determining the value of the resulting extract of malt. Some of the most extensively advertised and popular extracts of malt are practically without amylolytic action.—*Bull. Pharm.*, Detroit, 1905, v. 19, p. 494.

FERRI CARBONAS SACCHARATUS.

Gadd, Sydney C., contributes some laboratory notes on the manufacture of ferrous carbonate, the object being to supply a demand for a preparation which shall have the effect of Blaud's pills without their bulk. The method outlined is based on that given in the U. S. P. for the preparation of saccharated ferrous carbonate.—*Pharm. J.*, Lond., 1905, v. 21, p. 134.

FERRI CHLORIDUM.

Lyons, A. B., points out that while ferric chloride, U. S. P., VIII, should contain 25 per cent of iron, the official requirement is for only 22 per cent.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

Duncan, William, discusses a method for overcoming the incompatibility of ferric chloride with readily oxidizable bodies such as the alkali iodides.—*Pharm. J.*, Lond., 1905, v. 21, p. 861.

Moreau (*Bull. Soc. Pharm.*) presents a method for the volumetric titration of ferric chloride solution, based on the reaction between ferric chloride and sodium thiosulphate and the fact that only ferric salts give a violet reaction with salicylates.—*Year Book of Pharm.*, Lond., 1905, p. 81.

FERRI ET AMMONII CITRAS.

Siboni, G., discusses the composition of the several citrates of iron and of citrate of iron with ammonia, also the per cent content of iron.—*Apoth. Ztg.*, 1905, v. 20, p. 1018.

FERRI LACTAS.

Herting, Otto, does not appreciate the reason for dismissing lactate of iron from the pharmacopœia.—Deut.-Amer. Apoth. Ztg., N. Y., v. 26, 1905, p. 71.

FERRI SULPHAS EXSICCATUS.

Cowley, R. C., asserts that it is quite impossible to prepare the dried sulphate of iron pure and free from oxide (quite soluble), unless the salt is dried rapidly, and this method, too, is also somewhat objectionable because it liquefies the product and necessitates powdering for the final drying.—Brit. & Col., Druggist, 1905, v. 48, p. 382.

FERRUM.**SCALE PREPARATIONS.**

Cowley, R. C., takes exception to the way that scale preparations of iron have been treated in the U. S. P., VIII. He says:

They are all purely pharmaceutical preparations, and are yet introduced into a pharmacopœia without giving any instructions as to how they are to be prepared.—Brit. & Col. Drugg., Lond., 1905, v. 48, p. 382.

Sayre, L. E., believes that the omission of processes and methods of manufacture of the scale salts of iron, from the pharmacopœia, is a disadvantage.—Pharm. Era, N. Y., 1905, v. 34, p. 412.

TESTS FOR IRON.

Leather, J. W., discusses the precise determination of small quantities of iron by means of Lovibond's tintometer.—J. Soc. Chem. Ind., Lond., 1905, v. 24, pp. 385-387.

van Itallie, J., reports making some experiments to determine whether time and heat materially affect the accuracy of the method adopted by the German Pharmacopœia for the estimation of iron. He finds that while heating the solution to 50° C. has no material influence on the end result, time did slightly influence the sum total.—Pharm. Ztg., Berlin, 1905, v. 50, p. 1009.

Baxter and Frevert outline a method for the accurate estimation of ferrous iron, by titration with permanganate in the presence of hydrochloric acid and a manganous salt.—Am. Chem. J., 1905, v. 34, pp. 109-117.

Dunlop, Thomas, points out that a previously unnoted color reaction with glycerin is a characteristic test for ferric nitrate in the official ferric solutions.—Pharm. J., Lond., 1905, v. 21, p. 247.

ORGANIC IRON PREPARATIONS.

Dunning, H. A. B., discusses the several classes of formulas proposed for the preparation of a solution of iron and manganese pep-

tonate, and publishes a formula with detailed directions.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 397–401.

Beuttner, E. (*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 490), discusses the preparation of albuminate of iron solutions, and publishes a formula for a satisfactory and stable solution.—*Abstr. in Merck's Rep.*, N. Y., 1905, v. 14, p. 280.

A communication, signed "tz," contains formulas for the preparation of liquor ferri peptonati, liquor ferri albuminati, and liquor ferri oxydati saccharati neutralis.—*Pharm. Zentralh.*, 1905, v. 46, p. 856.

Tarozzi, G. (*Boll. chim. farm.*, 1905, No. 12), describes a method for making an ammoniated iron and manganese citrate with albumin that is said to be readily soluble in all proportions in cold water.—*Pharm. Ztg.*, 1905, v. 50, p. 671.

ACTION AND USES OF IRON.

Baldoni, Alessandro, records a series of investigations undertaken to demonstrate that iron is an essential constituent of the animal organism apart from the blood.—*Arch. f. expt. Path. u. Pharmacol.*, 1905, v. 52, pp. 61–68.

An editorial discusses the abuses which have arisen through the publication of garbled reports of scientific work, in connection with the use of iron as a therapeutic agent.—*J. Am. M. Ass.*, Chicago, 1905, v. 45, p. 1091.

Price, Eldridge C., presents a study of the use of iron as a food and as a therapeutic agent, together with an examination into its primary and secondary pathogenetic effects and their relation to disease.—*Tr. Am. Inst. Homœop.*, 1905, pp. 379–388. Also Hahne-mann. *Month. Phila.*, 1905, v. 40, pp. 561–572.

FERRUM REDUCTUM.

Lyons, A. B., asserts that the note appended to the assay process (p. 164, U. S. P., VIII) for reduced iron is not intelligibly expressed. The note might read—

The percentage purity of the iodine employed should be accurately determined by a previous experiment, and the weight of the iodine taken corrected accordingly before dividing by 0.02518 in the above calculation.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

Christensen (*Ztschr. f. anal. Chem.*, 1905) prefers the older method of estimating the iron in reduced iron, by the ferric chloride method, and outlines a modification of this reaction which he believes overcomes the objections formerly held.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 672.

Cormimbœuf and Grosman outline a method for the estimation of the iron content of reduced iron which is essentially similar to that given in the U. S. P., VIII.—Ann. de Chim. Analyt., 1905, v. 10, pp. 420-422.

Hartwich, C., calls attention to the readiness with which oxidation takes place in reduced iron and records a number of experiments made to determine the rapidity of change, under varying conditions.—Pharm. Ztg., Berlin, 1905, v. 50, p. 750.

Hill and Umney (Pharm. J., Lond., v. 19, p. 500) discuss the detection of arsenic in reduced iron. They propose a method based on the Ph. Germ., IV, and point out that the limitation proposed by Dunstan and Robinson, 60 parts per million, is not a practical one.—Year Book of Pharmacy, Lond., 1905, p. 42.

Alcock, F. H. (Pharm. J., Lond., v. 19, p. 852), asserts that while commercial samples are practically free from arsenic they leave a residue when treated with HCl; one leaving 2.75 per cent and another 7.5 per cent of apparently siliceous matter.—Year Book of Pharmacy, Lond., 1905, p. 82.

FICUS.

Eberle, E. G., enumerates *Ficus carica* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

FLUIDEXTRACTA.

An editorial review of the U. S. P., VIII, says:

The cumbersome nomenclature of the fluid extracts is simplified and they are now all written "Fluidextractum," thus avoiding the possibility of an error on the dispenser's part should the "Fluidum" be omitted by the prescriber.—Med. News, 1905, v. 87, p. 362.

In a review of the U. S. P., the assertion is made, that—

The introduction of the designation "Fluidextractum" in place of the more widely used Extractum Fluidum is an innovation that should not be followed.—Pharm. Ztg., Berlin, 1905, v. 50, p. 701.

"Xrayser" in discussing the new Latin of the U. S. P., VIII, says:

Fluidextractum can hardly be Augustan. We may expect Unitedstatesum next. A single word to represent the class of galenicals is, perhaps, a desideratum, but the nation which has invented "vaseline," "tabloid," and "liquozone," need not have been floored by such a simple problem.—Chem. & Drug., Lond., 1905, v. 67, p. 89.

An editorial comment on the U. S. P., VIII, says:

The new name for the old extracta fluida is one which will not appeal to purists in nomenclature.—Drug Topics, N. Y., 1905, v. 20, p. 197.

An editorial comment says:

A new word is coined of which we question the real advisability or the need. Instead of the former designation "Extractum Fluidum" it is now called "Fluidextractum."—Canad. Drug., 1905, v. 17, p. 347.

Wilbert, M. I., believes that the production of such lexicographic monstrosities as "Fluidextractum" and "Fluidextract" should require a more satisfactory apology than the feeble one offered in the preface of the pharmacopœia, particularly in view of the fact that the instructions given by the national convention of 1900 distinctly "recommend that changes in the titles at present official be made only for the purpose of insuring greater accuracy or safety in dispensing."—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 359.

The Spanish Pharmacopœia classifies the official extracts under the prefixes "Extractum aquosum," "Extractum alcoholicum," "Extractum æthereum," and "Extractum fluidum;" in the latter class there are but two representatives, fluid extract of hamamelis leaf and fluid extract of hydrastis.—*Farmacopea Oficial Española*, 1905, pp. 289-307.

An abstract (from J. Am. M. Ass.) asserts that the first fluid extract, of the kind now familiar to us, was made by William Procter, jr., of Philadelphia, who published a process for making fluid extract of ergot in 1857.—*The New Idea*, v. 27, 1905, p. 106.

Lyons, A. B., believes that there should be a distinctive title for the acetic fluid extracts.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 262.

Bollinger, George, points out that dilutions of fluid extracts should never take the place of U. S. P. tinctures. He believes that the two are not identical and that a tincture prepared from a fluid extract frequently precipitates.—*Pharm. Era*, N. Y., 1905, v. 34, p. 580.

FENICULUM.

Eberle, E. G., enumerates fennel as being among the medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 304.

Spaeth, E., points out that the commercial varieties of fennel should be enumerated in an official description, and that adulteration with extracted fruit should be guarded against. He also enumerates several simple tests by means of which extracted and artificially colored fruit may be recognized. He proposes the following requirements:

Fennel should consist of the undamaged fruit that has not been wholly or in part deprived of its essential oil, and should have a strong characteristic odor and taste of fennel. The ash should not exceed 10 per cent, and the portion insoluble in 10 per cent hydrochloric acid should not exceed 2.5 per cent.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, Berlin, 1905, v. 10, p. 21.

FRANGULA.

Mitlacher, W., reports on a sample of spurious frangula bark that came to his attention, and describes the bark, which he suggests may be derived from *Rhamnus carniolica*.—*Pharm. Post.*, Wien, 1905, v. 38, p. 751.

Warin, M. J., presents a comparative study of the oxymethylan-thraquinone content of the fluid extract of cascara and of fluid extract of frangula. The latter he found to contain from 7.55 to 7.60 gm. per kilo; the former, on the other hand, was found to contain from 5.90 to 5.95 gm. per kilo.—*J. de Pharm. et de Chim.*, Paris, 1905, v. 22, p. 12.

Vanderkleed, Charles E., outlines a method of assay for emodin-yielding drugs.—*Proc. Penna. Pharm. Ass.*, 1905, p. 193.

Panchaud, Adelp., has examined a number of samples of frangula and finds that young bark is invariably richer in emodin than the older bark. The emodin content in the several samples varied from 1.0 to 3.8 per cent in selected young bark. The determinations were made according to the method devised by Tschirch.—*Schweiz. Wehnschr. f. Chem. u. Phar.*, 1905, v. 43, p. 518.

GALLA.

Hartwich, C., presents a review of the literature relating to the uses and the composition of the galls of a number of trees and plants, including juniper, oak, rhus, eucalyptus, rhododendron, and sage. The article is illustrated by figures of the several galls that are discussed.—*Arch. d. Pharm.*, Berlin, 1905, v. 243, p. 584.

GAMBIR.

Nixon, C. F., in discussing the relative value of catechu and gambir, says: "Gambir, the old discarded pale catechu, has been added, with a requirement of 70 per cent soluble in alcohol. The leading importing houses are unable to furnish it even of this poor quality," and finally asserts that "Catechu of the market is richer in tannin than is gambir."—*Apothecary*, Boston, 1905, v. 17, p. 774.

Greshoff, M. (*Pharm. Weekblad*, v. 42, p. 699), reports a series of experiments on the assay of gambir.—*Abstr. in Pharm. J.*, Lond., 1905, v. 21, p. 657.

GELATINUM.

Klose, Curt, outlines a method for preparing a solution of gelatin, 1-8, that will remain liquid at ordinary temperatures. He directs that the solution be heated in a sterilizing apparatus for six hours, filtered, allowed to cool, and then reheated for one hour each day on three successive days. The resulting solution will keep well and may be dispensed to advantage, flavored with syrup of orange made slightly acid with citric acid.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 813.

Mann and Herzberg (*Therap. d. Gegenw.*, v. 46, No. 11) discuss the use of fluid gelatin in diarrhœa.—*Abstr. in J. Am. M. Ass.*, 1906, v. 46, p. 166.

Landmann, G. (Mitteilung. a. d. Grenzgebieten d. Med. u. Chir., Jena, v. 14, pp. 682-693) discusses the action of gelatin on the coagulability of the blood.—Reference from Ind. Med., 1905, p. 844.

GELSEMIUM.

Eberle, E. G., enumerates gelsemium as being one of the medicinal plants found in Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Lloyd, John Uri, in drug study No. 9, points out that while gelsemium is not usually adulterated, it is likely to be of inferior quality.—Pharm. Rev., 1905, v. 23, p. 329.

Sayre, L. E., presents a comparative study of the fresh and dry root and rhizome. He points out that the difference in alkaloidal content may be accounted for in bark relationship, all of the alkaloid being found in the bark. Sayre believes it probable that the alkaloid gelsemine is composed of two alkaloids, and that they may be separated by their difference in solubility in dilute acids.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 282-285.

Havenhill, L. D., reports finding a sample of gelsemium containing 15.13 per cent of ash, 7.5 per cent of moisture; two-thirds of the ash was sand. A reasonable limit for ash would be 3 per cent.—Proc. Kansas Pharm. Ass., 1905, p. 91.

Vanderkleed, Charles E., reports seven assays of gelsemium varying from 0.244 to 0.66 per cent of gelsemine. Two of the samples were below an average standard (4 per cent) for good drug.—Proc. Penna. Pharm. Ass., 1905, p. 56.

GENTIANA.

Gadd and Gadd assert that adulterations of gentian are most readily detected by means of the microscope, but that good evidence of quality is also furnished by the yield of extract, which should be about 40 per cent.—Pharm. J., Lond., 1905, v. 21, p. 439.

The revisors of Vienna pharmacies report finding gentian, particularly powdered gentian, contaminated with the root of *Gentiana asclepiadea*.—Pharm. Prax., 1905, v. 4, p. 38.

Tanret, Georges, contributes several papers on the active principles and the constituents of gentian, one on gentiopicrin and another on gentiine.—Compt. rend. Acad. d. sc. Par., v. 141, 1905, pp. 207-209, 263-264.

Alcock, F. H., suggests that the diversity of opinion about the percentage of total solids in the compound tincture of gentian is really due to the variation in the gentian itself, and points out that a careful selection of gentian is needed if concordant results are to be obtained.—Pharm. J., Lond., 1905, v. 21, p. 128.

Beringer, George M., gives detailed directions for the preparation of a fluid extract of gentian by the infusion process.—Pharm. Era, N. Y., 1905, v. 34, p. 30.

GLANDULÆ SUPRARENALES SICCÆ.

Thornton, E. Q., points out that the U. S. P., VIII, contains no assay process nor does it provide for the physiological testing of either the suprarenal or thyroid products.—*Therap. Gaz.*, Detroit, 1905, v. 29, p. 736.

Meltzer and Auer discuss the influence of suprarenal extract, in the form of the active principle, upon absorption and transudation. They believe that their results indicate that (1) intravenous injections of suprarenal extract invariably retard the processes of absorption and transudation; (2) subcutaneous injections also often show a retardation of these processes of absorption and transudation; (3) in frogs the retardation of absorption was recognizable only when the substance was injected with the suprarenal extract—*Am. J. M. Sc.*, v. 129, pp. 114-129.

Douglass, Beaman, presents a comprehensive study of the action and the effects of the extracts and derivatives of the suprarenal glands on life processes.—*Ibid.*, pp. 98-114.

Floersheim, Samuel, discusses the present status of suprarenal therapy, gives some general references to the history of its introduction, and the conditions in which it may prove of value.—*Med. News*, N. Y., 1905, v. 86, pp. 587-590.

See also under *Epinephrina*.

GLANDULÆ THYROIDEÆ SICCÆ.

Hunt and Motter call attention to the several so-called active constituents of the thyroid that are now on the market, and also call attention to a series of preparations whose action is stated to be quite opposite to that of thyroid, and which are prepared from the blood or the milk of animals from which the thyroids have been removed.—*Bull. No. 23, Hyg. Lab. U. S. P. H. and M.-H. S.*, 1905, p. 39.

Hunt, Reid, reports a series of investigations with the feeding of dried and powdered thyroid to white mice and the susceptibility of these animals to the toxic action of acetonitrile.—*J. of Biol. Chem.*, 1905, v. 1, pp. 33-44.

GLYCERINUM.

Havenhill, L. D., presents tabulated results of examination of eleven samples of glycerin.—*Proc. Kansas Pharm. Ass.*, 1905, p. 91.

An abstract from *La Revue de Chimie industrielle* (no date) presents quite a comprehensive description of the process for the manufacture of glycerin from the residue of distillation.—*Paint, Oil and Drug Rep.*, Aug. 14, 1905, p. 53.

van Itallie, E. J., discusses the control of glycerin and the proposal made by van Smithen to estimate the glycerin content by the specific gravity.—*Pharm. Weekbl.*, 1905, v. 42, pp. 269-271.

Schulze, Fr., elaborates on a former contribution and gives his results with the several methods for estimating glycerin in fats and oils in soaps and in glycerin preparations.—*Chem. Ztg. Cöthen*, 1905, v. 29, p. 976.

Strauss, H., outlines a method for the determination of glycerol in soap lyes, based on the oxidation of the glycerol by means of potassium bichromate and sulphuric acid.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 1128 (from *Chem. Ztg. Cöthen*).

Shukoff and Schestakoff (*Ztschr. f. angew. Chem.*, 1905, v. 18, p. 294) outline a method for the direct determination of glycerin in solutions.—*Abstr. in Pharm. J., Lond.*, 1905, v. 21, p. 761.

Pope, Lester, criticises the use of glycerin in ointments and suggests the use of castor oil in preference.—*Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 396.

GLYCERITA.

Caldwell, Paul, asserts that it is difficult so to regulate the heat in making glycerite of boroglycerin as to keep the finished product from having a distinct brown color. He believes a vacuum pan is essential for the successful production of this preparation. He believes it impracticable for the retail druggist to make glycerite of hydrastis, on account of the cost. He suggests the use of an alternative formula and the introduction of an alcoholic extract of hydrastis.—*Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 306.

Hommell, P. E., recommends a glycerite of elm bark as a vehicle for bismuth salts, chalk, magnesia, and a number of other substances where a demulcent, mucilaginous vehicle is desirable. He recommends the following formula: Slippery elm bark, 10 parts; glycerin, 25 parts; water, a sufficient quantity to make 100 parts. Boil the bark with the water for five minutes, macerate two hours, strain, and add water enough to make 75 parts, add the glycerin, and filter.—*Apothecary, Boston*, 1905, v. 17, p. 616.

"A Junior Pharmacist" points out that the easiest, though not the most rapid, way to make glycerite of tannic acid is to weigh and mix the ingredients and allow to stand in the cold, with occasional agitation. This preparation requires two or three days for complete solution.—*Pharm. J., Lond.*, 1905, v. 21, p. 462.

GLYCYRRHIZA.

True, Rodney H., mentions the fact that the licorice plant thrives in various localities in this country, and points out the possibility of growing it on a commercial scale.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 273.

Gadd and Gadd point out that while microscopic examination is the best indication of quality the determination of ash is a ready, if

rough, test, and point out that 100 parts should not leave more than 4 parts of ash. Compound licorice powder, treated similarly should yield not more than 5 per cent of ash.—Pharm. J., Lond., 1905, v. 21, p. 438.

Beringer, George M., recommends a modification of the infusion process for making fluid extract of glycyrrhiza. He proposes the following formula: Glycyrrhiza in coarse powder, 1,000 gm., ammonia water, 50 cc., alcohol and water, of each a sufficient quantity to make 1,000 cc. Mix the ammonia water with sufficient water to make 1,000 cc., and having mixed the ground drug with 700 cc. of this mixture, pack it in a cylindrical percolator; then add enough menstruum to saturate the drug and leave a stratum above it. Macerate for forty-eight hours, then percolate, completing the exhaustion of the drug with water. Reserve the first 500 cc. of the percolate and add to it 250 cc. of alcohol. Evaporate the remainder of the percolate to a soft extract, dissolve this in the reserved portion and allow to stand for two or three days, then filter and wash the filter with a mixture of alcohol 1 volume and water 3 volumes to make the fluid extract measure 1,000 cc.—Pharm. Era, N. Y., 1905, v. 34, p. 29.

Pégurier, Gaston, suggests the introduction of fluid extract of glycyrrhiza into French pharmacies, and recommends it highly for masking the taste of such drugs as cascara and hydrastis.—Bull. Sc. Pharmacol., Paris, 1905, v. 12, pp. 211-212.

Guiges, P., discusses the fluid extract of glycyrrhiza.—*Ibid.*, pp. 332-334.

Seltzer, Leonard A., outlines a process for making a stable and elegant syrup of glycyrrhiza, using egg albumen and heat to clarify the solution, which is then directed to be filtered through paper pulp. Pharm. Era, N. Y., 1905, v. 34, p. 175.

Kebler, Lyman F., reports finding ground olive stones in compound licorice powder.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 185.

An editorial comments on the inferior quality of the extract of glycyrrhiza found on the market, and cites 12 samples of powdered extract, 8 of which contained more or less cornstarch. The insoluble residue in the total number of samples ranged from 18 to 34.3 per cent.—Am. Druggist, N. Y., 1905, v. 47, p. 7.

GLYCYRRHIZINUM AMMONIATUM.

The committee on adulterations reports that several samples of ammoniated glycyrrhizin purchased in the open market were practically insoluble in alcohol. The actual cause for this condition is to be reported on later.—Proc. Michigan Pharm. Ass., 1905, p. 78.

GOSSYPIMUM.

Eberle, E. G., mentions *Gossypium harbaceum* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Just's Botanischer Jahresbericht (for 1905, v. 33, pt. 3, pp. 759–768) contains upward of 140 references on the cultivation of cotton, the diseases and insects attacking the plant, and various methods for determining the value of cotton.

GRANATUM.

Eberle, E. G., mentions *Punica granatum* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Dohme, A. R. L., believes that the alkaloid content of pomegranate root varies but little. For five years, 1899 to 1903, the highest average reported was in 1900, 0.7 per cent, while the lowest, 1903, was 0.48 per cent.—Apothecary, Boston, 1905, v. 17, p. 942.

Lloyd, John Uri, asserts that the rind of the fruit and the bark of the tree, as well as the bark of the root have all been distributed under the name Pomegranate bark, for which the root bark alone should be used. He questions if drug dealers make any efforts whatever to differentiate between the bark of the different varieties of pomegranate, or whether it be obtained from the wild or the cultivated tree.—Pharm. Rev., 1905, v. 23, p. 329.

Caeser and Loretz outline a method for the titrimetric as well as the gravimetric determination of the alkaloids present in pomegranate root bark.—Geschäfts-Ber. von Caeser & Loretz, in Halle a. S., 1905, pp. 81–83.

GRINDELIA.

Eberle, E. G., mentions *Grindelia squarrosa* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

Power and Tutin present an exhaustive paper on the chemistry of *Grindelia robusta*. The authors conclude from their work that (1) the chief constituents of grindelia are amorphous resins, to which its medicinal value is probably to be attributed; (2) *Grindelia* contains a considerable amount of a lævo-rotatory sugar, apparently l-glucose; it also contains proteid substances, amorphous coloring matter and tannin, and an exceedingly small amount of an essential oil, possessing the characteristic odor of the drug; (3) they are unable to confirm the observations of previous investigators respecting the presence of a saponin or alkaloid.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 192–201.

Lloyd, John Uri, asserts that the shades of difference that separate *Grindelia robusta* and *Grindelia squarrosa* are so slight as to be scarcely a factor with commercial drug collectors. He also points

out that *Grindelia squarrosa* as such is not to be had on the general market. The demand is restricted and whoever obtains it must get it directly from an intelligent drug collector.—Pharm. Rev., 1905, v. 23, p. 329.

Cowperthwaite, A. C., points out that *Grindelia robusta* is used in asthma, bronchitis, whooping cough, and rhus poisoning, both internally and locally.—Tr. Am. Inst. Homœop., 1905, v. 61, p. 363.

GUAIACOL.

An abstract (from J. de Pharm. d'Anvers, 1905, No. 7) suggests the following formula for guaiacol pills: Guaiacol 1.0, powd. glycyrrhiza 1.0, potassium carbonate 0.25, glycerin a sufficient quantity. Mix and make into 25 pills.—Pharm. Ztg., Berlin, 1905, v. 50, p. 773.

Opikhamoff, P. A., has published a monograph (St. Petersburg, 1905) on the influence of guaiacol on the blood in cutaneous application.—Reference from Ind. Med., 1905, v. 3, p. 674.

Hecht (Münch. Med. Wchnschr., 1905, v. 52, p. 415) discusses the endermatic application of guaiacol.—*Ibid.*, p. 355.

Schüller, Max, discusses the use of guaiacol in the treatment of tuberculosis of the kidneys.—(From Mitteilungen a. d. Grenzgebiet. Jena, 1905, v. 15, Nos. 1 & 2.) Abstr. in J. Am. M. Ass., 1905, v. 45, p. 1613.

Cain, William George, discusses the use of guaiacol in the treatment of pneumonia.—Therap. Gaz., 1905, v. 29, pp. 436–437.

GUAIACUM.

Moore, Russell W., says that of 124 samples of guaiac examined for entry into the port of New York, 69 were below the standard of 80 per cent resin. The maximum was 91.4 per cent and the minimum 61.7 per cent, the average being 77.92 per cent.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 266.

Petit and Meyer (Compt.-rend., 1905, v. 141, pp. 193–195) discuss the several reactions of guaiac and point out among other facts that the tincture of guaiac gives a very strong blue coloration with iron or manganese salts.—Abstr. in J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 655.

Gadd and Gadd assert that 110 minims of ammoniated tincture of guaiac (Ph. Brit., IV) evaporated on a water bath for three hours should yield a residue of not less than 15 grains.—Pharm. J., Lond., 1905, v. 21, p. 579.

Caldwell, Paul, suggests that in making the ammoniated tincture of guaiac a more purely alcoholic menstruum be used, to which the oils and an equivalent amount of spirit of ammonia might be added.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 306.

GUARANA.

Vanderkleed, Charles E., reports 3 assays of guarana which varied from 3.45 to 4.91 per cent of caffeine.—Proc. Penna. Pharm. Ass., 1905, p. 56.

Dohme, A. R. L., reports that the alkaloid content of guarana varied from an average of 3.75 per cent in 1902 to an average of 4.18 per cent in 1904.—Apothecary, Boston, 1905, v. 17, p. 942.

Lyons, A. B., points out that in the assays of guarana and of its fluid extract, provision is made for the extraction of other alkaloids as well as caffeine (as in the case of kola), and the expression "alkaloids from guarana" is used in place of caffeine. In fact guarana is not known to contain any alkaloid except caffeine.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 261.

HAMAMELIDIS CORTEX.

Eberle, E. G., mentions *Hamamelis virginiana* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

AQUA HAMAMELIDIS.

LaWall, Charles H., found 15 samples of distilled extract of witch hazel, all of which contained formaldehyde, and one sample which contained wood alcohol. The alcohol strength varied from 9 to 13 per cent by volume.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 190.

Brooks, C. H., tested 21 samples, and of these 5, or 23.2 per cent, contained wood alcohol. The alcoholic percentage varied from 5.5 to 14.5.—Proc. Massachusetts Pharm. Ass., 1905, p. 105.

Francis, John M., points out that the official directions for hamamelis water are practically useless, as the manufacture of this product is entirely in the hands of large distillers. He asserts that there is much inferior distilled extract of witch hazel sold, some of it having so little of the characteristic odor as to be hardly recognizable as such. Apart from the tests for wood alcohol and formaldehyde, he believes that one can not go amiss by simply pouring the liquid on the hands or face, as the barber does, and thus providing a really practical test.—Bull. Pharm., Detroit, 1905, v. 19, p. 361.

Lloyd, John Uri, discusses the properties and uses of the distilled preparation of witch hazel and of the astringent percolate extractive, and points out that the two are not infrequently substituted one for the other.—Pharm. Rev., 1905, v. 23, p. 329.

Katz, J., reviews the description for hamamelis water, as given in the German Homœopathic Pharmacopœia by Wilmar Schwabe, and records some experiments with a modification of the process recorded in that book.—Pharm. Ztg., Berlin, 1905, v. 50, p. 642.

HEDEOMA.

True, Rodney H., reports that hedeoma is grown regularly in the testing gardens of the U. S. Department of Agriculture.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 275.

The Bureau of Plant Industry recommends planting hedeoma seed in the autumn.—Ann. Rep. Dept. Agric., 1905, p. 147.

HEXAMETHYLENAMINA.

Caldwell, Paul, says of the name "Hexamethylenamina:"

This is one of the things in the new pharmacopœia which gives a dignified air but which seems to disinherit the average physician so far as any benefit to be derived from the use of the book is concerned.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 306.

Wöhlk, Alfred, suggests the use of Nessler's reagent for the detection of ammonia, amides, and paraformaldehydes in hexamethylenamine. He asserts that hexamethylenamine itself, even on boiling with solution of sodium hydroxide, does not liberate even a trace of nitrogen in the form of ammonia.—Ztschr. f. analyt. Chem., 1905, v. 44, pp. 765-766.

Lubowski, M. (from Therapist, Lond., 1904, pp. 114-131) presents a comprehensive review of the literature of urotropine and its therapeutic significance.—Reference from Ind. Med., 1905, p. 257.

HUMULUS.

A review of the use of hops (Ber. Vers. Anst. Brauindus. Böhmen, 1905, No. 11, p. 40) presents facts relating to the volatile oils, resins, and hop acids in several varieties of hops.—Reference from Exp. Sta. Rec., 1905, v. 17, p. 858.

Eberle, E. G., mentions *Humulus lupulus* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

HYDRARGYRI CHLORIDUM CORROSIVUM.

Vanderkleed, Charles E., examined twelve lots of mercuric chloride during the past year. Two of these lots contained calomel.—Proc. Penna. Pharm. Ass., 1905, p. 53.

Rupp, E., outlines a method for the determination of mercuric chloride in pastilles which is designed to overcome the disturbing effect of the sodium chloride that may be present.—Pharm. Ztg., Berlin, 1905, v. 50, p. 561.

Utz outlines a method for applying the tests proposed by Rupp for determining the quantity of mercuric chloride in surgical dressings.—Apoth. Ztg., Berlin, 1905, v. 20, p. 702.

Eberle, E. G., believes that mercuric chloride tablets may be advantageously made with sodium chloride in place of the ammonium chloride. When a tablet containing the latter is dissolved in ordinary water a precipitate is formed, owing to the presence of calcium carbonate. There is no precipitate when sodium chloride is used to effect the solution.—*Apothecary*, Boston, 1905, v. 17, p. 951.

Fiora, Paola, reports some experiments made to determine the amount of boric acid necessary to overcome the incompatibility between mercuric chloride and cocaine hydrochloride. He suggests the use of 3 per cent of boric acid with one-half per cent each of mercuric chloride and cocaine.—*Bull. Chim. Farm.*, Milan, 1905, v. 44, pp. 380–381.

HYDRARGYRI CHLORIDUM MITE.

Caspari, Charles E., examined 157 samples of calomel; 82 of these samples contained minute quantities of mercuric chloride, while the other 75 samples were absolutely pure.—*Proc. Missouri Pharm. Ass.*, 1905, p. 75.

Havenhill, L. D., found 4 samples which contained traces of mercuric chloride.—*Proc. Kansas Pharm. Ass.*, 1905, p. 91.

Vanderkleed, Charles E., examined 16 lots of calomel, only 8 of which were found to be absolutely free from mercuric chloride, but in no case was the amount of the latter sufficient to cause harm. He points out that since 50 per cent of the samples did comply with the U. S. P. requirements in this particular, this requirement is not too strict.—*Proc. Penna. Pharm. Ass.*, 1905, p. 53.

Wijne (*Pharm. Ztg.*, 1905, v. 50, p. 369), found crystals in the powder of calomel and believes that unpleasant consequences might result from the use of such a preparation, particularly in the eye. He thinks the formation of these crystals was due to gradual accumulation on the bottom of storage vessels.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 739.

Meyer, J. (from *Z. anorg. Chem.*, 1905), calls attention to a modification of calomel obtained from a mixture of mercuric chloride and a solution of lithium sulphite as a secondary product. This new product he believes to be identical with the Japanese calomel described by Lunge and Divers.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 1255.

An editorial note discusses the incompatibility of mercurous chloride with antipyrine, and points out that, in place of its being due to the formation of mercuric chloride, it is in reality due to a complex reaction in the course of which an organic mercurous salt is decomposed into mercuric chloride.—*Pharm. Prax.*, 1905, v. 4, p. 468.

HYDRARGYRI IODIDUM FLAVUM.

Szilard, B. (from Gyogyzs Ertes, 1905, No. 46), suggests that mercurous iodide may be readily prepared by shaking the mercury with chloroform and gradually adding the iodine previously dissolved in another portion of chloroform. The reaction progresses rapidly, and should, therefore, be conducted with care; the resulting iodide may be washed in the usual way.—Pharm. Ztg., Berlin, 1905, v. 50, p. 1009.

HYDRARGYRI IODIDUM RUBRUM.

Penzoldt, F., reviews the use of mercuric iodide in solution with potassium, and commends the use of this simple and generally efficacious combination.—Therap. d. Gegenw., 1905, v. 7, pp. 23–25.

HYDRARGYRI OXIDUM FLAVUM.

Pinchbeck, G., presents a number of interesting facts dealing with the history of the introduction of yellow mercuric oxide into ophthalmic practice. In connection with this discussion he suggests the following general formula: Yellow mercuric oxide, 0.1 to 1.0; anhydrous wool fat, 1.0; spermaceti ointment, or paraffin, a sufficient quantity to make 10.0.—Pharm. J., Lond., 1905, v. 21, p. 359.

Knapp recommends that for the preparation of the ointment of yellow mercuric oxide a freshly precipitated yellow oxide be used, and suggests that the water may be eliminated by washing first with water, then alcohol, and finally ether, and allowing the latter to evaporate.—Bull. Sc. Pharmacol., Paris, 1905, v. 12, p. 18.

HYDRARGYRUM.

Rupp and Nöll record some experiments to adapt a thiocyanate solution to the titrimetric determination of mercury in organic combinations. They outline a method that has been adapted to the salicylate and the succinimide of mercury.—Arch. d. Pharm., 1905, v. 243, pp. 1–5.

Rupp, E., outlines a method for the titrimetric determination of mercury by reducing the respective salts by means of formaldehyde and soda solution, converting the mercury to iodide and titrating the superfluous iodine with sodium hyposulphite.—*Ibid.*, p. 300.

Tarugi, N., points out that by the action of mercury vapor on metallic aluminum, aluminum amalgam is formed, and that this reaction may serve as a sensitive test for mercury.—J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 334 (from Gaz. chim. Ital., 1905, v. 34, pp. 486–492).

HYDRARGYRUM AMMONIATUM.

Allen reports finding samples of ammoniated mercury which failed to comply with the requirements of the official standard.—Proc. Michigan Pharm. Ass., 1905, p. 80.

HYDRASTIS.

Henkel and Klugh (U. S. Dept. Agr., Bureau of Plant Industry, Bul. 51) give notes on the identification, distribution, and cultivation of golden seal, also some reference to the methods of collecting and preparing the rhizomes for the market. It is shown that under artificial shade the plant can be cultivated without much difficulty.—Exper. Stat. Rec., 1905, v. 16, p. 747.

Henkel, Alice, presents a study of the nature, uses, and experiments with the cultivation of golden seal.—Western Drugg., Chicago, 1905, v. 16, p. 747.

True, Rodney H., asserts that golden seal culture is now a practicable garden proposition.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 275.

A similar assertion is made by the Bureau of Plant Industry.—Ann. Rep. U. S. Dept. Agric., 1905, p. 147.

Lloyd, John Uri, reports an experiment in hydrastis culture and asserts that *Hydrastis canadensis* is a very easy crop to raise by transplanting the entire root.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 307-310.

Warren, Northam, discusses the propagation and the growing of hydrastis. Appended to the article are the names of a number of people interested in the cultivation of this plant.—Bull. Phar., Detroit, 1905, v. 19, p. 323.

Caeser and Loretz assert that the experiments made in the cultivation of hydrastis have as yet not sufficiently progressed to be of commercial importance. The available supply of the drug is practically exhausted, and fresh supplies are limited.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 621.

Hood, C. S., presents some reference to the history and the origin of hydrastis.—West. Drugg., 1905, v. 27, p. 773.

Lloyd, John Uri, asserts that every drug, native to the soil, that resembles this rhizome, either in fiber or in color, has been known to be mixed with it. He also enumerates a number of root drugs that have been found admixed with or substituted for hydrastis.—Pharm. Rev., 1905, v. 23, p. 330.

Vanderkleed, Charles E., finds that nine assays varied from 1.80 to 3.45 per cent of hydrastine. Two samples of the powdered drug assayed below 2.25 per cent of hydrastine.—Proc. Penna. Pharm. Ass., 1905, p. 56.

Dohme, A. R. L., asserts that the quality of hydrastis improved steadily from 1899 to 1902 and then gradually began decreasing again. He also asserts that the spring root is better than the fall root, and gives the average alkaloid content for the years 1899 to 1905, inclusive.—Apothecary, Boston, 1905, v. 17, p. 942.

Hartwich and Hellström (Apoth. Ztg.) give a key according to which, they assert, it is quite possible to recognize the several roots that have been employed as adulterants of hydrastis.—Pharm. Prax., 1905, v. 4, p. 229.

The committee on adulterations found a sample of extract of hydrastis which contained, as a diluent and absorbent, infusorial or siliceous earth.—Proc. Michigan Pharm. Ass., 1905, p. 79.

Caeser and Loretz suggest a method for the assay of hydrastis in which they recommend a mixture of 100 gms. of ether and 20 gms. of benzine as a solvent.—Geschäfts-Ber. v. Caeser & Loretz, in Halle a. S., 1905, p. 96.

Maben, Thomas, believes that the allowance for a loss of 20 per cent of the alkaloid in the manufacture of the fluid extract appears to be excessive.—Pharm J., Lond., 1905, v. 21, p. 141.

Koning, J. (from Pharm. Weekbl., 1905, No. 42), examined 8 different samples of extracts of hydrastis and found but 2 which complied with the requirements of Ph. Germ., IV, for alkaloid.—Pharm. Ztg., Berlin, 1905, v. 50, p. 919.

Newton, C. H. W., gives some historical notes and several formulas for preparations of hydrastis.—Proc. Connecticut Pharm. Ass., 1905, pp. 39-42.

Hammer, J. W., discusses the formula for fluid extract of hydrastis, included in Ph. Svec., VIII, and the extract content.—Svensk. Farm. Tidskr., 1905, v. 9, pp. 65-67.

Crance, A. J., points out that—

The specific affinity of hydrastis in disease expression is that of a mucous membrane tonic. * * * The specific indications are an increased secretion from mucous surfaces with atony, as evidenced by impaired circulation and innervation.—Eclectic M. J., 1905, v. 65, pp. 203-205.

See also Snyder, George.—*Ibid.*, p. 376.

An abstract asserts that hydrastis, while it is quite rapidly eliminated from the body if the kidneys are in a healthy condition, may accumulate in the system in chronic interstitial nephritis and produce a series of symptoms, among them headache, vertigo, blurred vision, nausea, constipation, and convulsions.—Hahneman. Month., Phila., 1905, v. 40, p. 612.

HYOSCINÆ HYDROBROMIDUM.

Kobert, R., points out that the name "hyoscin" originated with Ladenburg, who applied it to a substance having a chemical formula

($C_{17}H_{23}NO_3$), which as yet has not been reproduced by any other investigator. As this formula differs from that found in what is usually called hyoscine, it is evident that the name should not be continued, and it has very properly been suggested to omit it entirely from future revisions of the German Pharmacopœia.—Riedel's *Berichte*, 1905, p. 11.

Hesse, O., discusses the presence of atroscein as a contamination of hyoscine.—*Suedd. Apoth. Ztg.*, 1905, v. 45, pp. 215–216.

Bering, R. E., discusses the use of hyoscine hydrobromate in morphine addiction (*California State Jour. of Med.*, July, 1905).—*Abstr. in J. Am. M. Ass.*, 1905, v. 45, p. 657.

See also Wagner, H. G.—(*Cleveland M. J.*, June, 1905.) *Abstr.*, *ibid.*, p. 355.

HYOSCYAMUS.

True, Rodney H., says that hyoscyamus has been successfully grown in the testing gardens of the Bureau of Plant Industry.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 274.

Rusby, H. H., asserts that much of the henbane of commerce is taken from the plant in the first year of its growth.—*Merck's Rep.*, N. Y., 1905, v. 14, p. 212.

Vanderkleed, Charles E., finds that 7 assays of henbane leaf varied from 0.078 to 0.251 per cent of alkaloids. He believes that the general quality of this drug is good.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 56.

Dohme, A. R. L., asserts that hyoscyamus runs fairly uniform in alkaloidal content. During the five years from 1901 to 1905, inclusive, the greatest variations were from 0.09 per cent in 1904 to 0.15 per cent in 1905. He also points out that henbane in 1905 is running unusually high, as high as 0.2 per cent alkaloid being quite common.—*Apothecary*, Boston, 1905, v. 17, p. 942.

The revisors of Vienna pharmacies assert that hyoscyamus leaves were frequently found with an abnormally high ash content. In one case the ash content amounted to no less than 64.5 per cent; other figures indicate the presence of from 16.5 to 23.3 per cent of ash, the average given in the literature being from 19 to 23 per cent.—*Pharm. Prax.*, 1905, v. 4, p. 37.

An abstract asserts that of two specimens of *Hyoscyamus muticus*, one, obtained from the Punjab, was found to contain 0.36 per cent of hyoscyamine in the dry stems, while the second, from Larkana, contained 0.28 per cent. In neither case was any other alkaloid detected. It is thought that these low alkaloid contents would indicate that the Indian plant can not compete with the richer Egyptian variety as a commercial source of hyoscyamine.—*Merck's Rep.*, 1905, v. 14, p. 214.

Naylor, W. A. H., points out that in devising a process for the estimation of total basic content in hyoscyamus leaves it is advisable that regard should be had to the ease with which hyoscyamine undergoes isomerisation. He also points out that, quite irrespective of whether or not a change in molecular constitution affects the therapeutic value of the alkaloid, it is desirable, from the chemist's standpoint, that any such alteration should be guarded against and, as far as possible, provisions be made accordingly in any process recommended for the assay of the drug or its preparations.—*Pharm. J., Lond.*, 1905, v. 21, p. 126.

Maben, Thomas, commends the standard adopted by the U. S. P., VIII, for hyoscyamus, as splitting the difference between that advocated by Farr and Wright and that by Maben.—*Ibid.*, p. 141.

Caeser and Loretz recommend the same modification for the U. S. P., VIII, as that given under Belladonna (q. v.).—*Pharm. Ztg., Berlin*, 1905, v. 50, p. 771.

Nixon, C. F., believes that pharmacists, as a class, will never be in a position to assay tincture of hyoscyamus for 0.007 per cent of alkaloids. This, he believes, calls for high skill, while the non-compliance with the requirement, on the other hand, will prove to be a great detriment to pharmacy.—*Apothecary, Boston*, 1905, v. 17, p. 774.

Rasthje, A., has studied the alkaloidal content of oil of hyoscyamus, as prepared by four different methods, and has endeavored to increase this alkaloidal content by the addition of a small quantity of stearic acid (from *J. de Pharm. v. Elsass-Lothr.*, 1905, p. 193).—*J. de Pharm. et de Chim., Paris*, 1905, v. 23, p. 65.

Kuntz, W., discusses the preparation of the infused hyoscyamus oil and describes a method by which he prepared an oil containing as high as 0.6 per cent of alkaloids. The editor calls attention to the wide discrepancy in the percentages given by the two writers and suggests the possibility of error.—*Ibid.*, p. 66.

INFUSA.

Currie, A., outlines a method for sterilizing infusions and offers some objections to Witte's method (from *Pharm. J., Lond.*, v. 20, p. 584).—*Year Book of Pharmacy, Lond.*, 1905, p. 258.

Deane, H. (*Pharm. J., Lond.*, v. 20, p. 435), criticizes the so-called concentrated infusions as being insufficiently extracted and gives a tabulated statement of his results.—*Ibid.*, pp. 259-261.

Pearson, G. E., controverts Deane's contention and gives an even more extensive tabulated statement (*Pharm. J., Lond.*, 1905, v. 20, p. 474).—*Abstr., ibid.*, p. 261.

The Spanish Pharmacopœia contains no less than 14 formulas for infusions, among them: Infusion of digitalis, rhubarb, arnica root,

senega, ipecacuanha, jaborandi, quassia, calumba, manna, and cinchona.—*Farmacopea Oficial Española*, 1905, pp. 355–359.

Zeisler deprecates the fact that even some of the leading manufacturers of fluid extracts in the country print on their labels formulas for the preparation of infusions from fluid extracts and believes that the practice should be discouraged.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 319.

iodoformum.

Siedler, P., points out that the Ph. Germ., IV, requires that iodoform have a melting point of about 120° C., and that under normal conditions it was found to melt at from 115° to 116° ; on more rapid heating it is possible to reach 120° before the material melts.—*Pharm. Post*, Wien, 1905, v. 38, p. 568.

Utz (*Pharm. Zentrallh.*, v. 45, pp. 985–987) outlines a method for the determination of iodoform, in which the iodoform is directed to be dissolved in a mixture of ether and methyl alcohol, treated with a few drops of fuming nitric acid and $\frac{1}{10}$ N. silver nitrate, the mixture heated, diluted, and finally titrated with ammonium thiocyanate solution.—*Abstr. in J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 353.

A somewhat similar process by M. Borri is noted in *Bull. des Sc. Pharmacol.*, 1905, v. 12, p. 19.

Schoorl and van den Berg discuss the changes that are brought about in iodoform under the influence of light, heat, and air. They enumerate the decomposition products and record some experiments carried out to determine the probable changes.—*Ber. d. pharm. Gesellsch.*, Berlin, 1905, v. 15, p. 398.

van Aubel, E. (*Phys. Ztg.* v. 5, p. 637), discusses the decomposition of iodoform by the combined action of light and oxygen. This decomposition takes place even in non-fluid mixtures (e. g., iodoform and vaseline) under the action of light, Röntgen rays, or of radium emanations.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 103.

Stevens, Luther F., outlines a method for the preparation of iodoform by the interaction of acetone and potassium iodide in the presence of sodium hydrate and solution of chlorinated soda.—*Proc. New York Pharm. Ass.*, 1905, pp. 92–94.

Rousch, G. A., discusses the electrolytic production of iodoform from acetone and points out that the electrolysis of potassium iodide and acetone without a diaphragm produces 2 molecules of alkali for each molecule of iodoform produced, whilst with a diaphragm 4 molecules of acid are obtained to each molecule of iodoform. He proposes a combination of the two reactions (from *Proc. Am. Electrochem. Soc.*, 1905).—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 1254.

Blanchi, A., recommends an extemporaneous preparation of iodoform prepared by mixing the following ingredients in the order

enumerated: Potassium hydrate, 35.0; distilled water, 25.0; oleic acid, 50.0; iodine, resublimed, 30.0; and alcohol, 95 per cent, 30.0. The resulting iodoform soap solution is said to be readily absorbed by the unbroken skin.—*Boll. Chim. Farm.*, 1905, v. 44, pp. 702-704.

Mulzer, P., presents an exhaustive discussion of the action of iodoform in the animal body and gives tabulated results of findings, both ante and post mortem.—*Ztschr. f. expt. Path. u. Therap.*, Berlin, 1905, v. 1, pp. 446-449.

IODUM.

Köthner and Auer discuss the work done by Stas, and some of the succeeding workers, in connection with the atomic weight of iodine, and report their experiments which lead them to believe that the atomic weight of iodine is 126.98 with $O = 16$.—*Liebigs Annal. d. Chem.*, v. 337, p. 169.

Ladenburg, A., offers some criticism on the report made in the above article, and Köthner, P., replies.—*Ibid.*, pp. 259-265.

Baxter, Gregory Paul (from *Proc. Am. Acad. of Arts and Sc.*, v. 40, p. 419), discusses the work previously done, the relation of silver to iodine, the purification of the materials used, the method of analysis, the relation of silver iodide to silver chloride, and finally gives as his conclusion that the atomic weight of iodine is 126.975 with $O = 16$.—*Ztschr. f. anorgan. Chem.*, 1905, v. 43, pp. 14-33.

Barbieri, Giuseppi, presents a note on the alkalimetric determination of iodine.—*Boll. Chim. Farm.*, Milano, 1905, v. 44, pp. 6-7.

Hennecke advises the titration of iodine in chloroform solution, instead of the usual aqueous potassium iodide solution, in order to avoid the decomposition of the iodine monochloride, which it may contain.—*Bull. des Sc. Pharmacol.*, Paris, 1905, v. 12, p. 16.

Thilo (*Chem. Ztg.*, v. 28, p. 866) outlines a method for the determination of iodine in the presence of bromine and chlorine, which is based upon the observation that the gradual addition of a silver salt solution to a solution containing all three halides will first precipitate the iodine, and that the latter will also convert silver bromide and chloride into iodide. The end point of the iodine precipitation, carried out with silver solution of known strength, is shown when a drop of the solution no longer gives a dark spot of palladinous iodide on filter paper freshly dipped into palladinous chloride solution.—*Abstr.*, *J. Am. Chem. Soc.*, 1905, v. 27, p. 1347.

Tatlock and Thomson outline a method for the determination of small proportions of bromine and of chlorine in iodine, in which they propose treating 5 to 10 gms. of the sample with 50 to 100 cc. of water and finely granulated or powdered zinc to convert all of the iodine into zinc iodide, care being taken not to allow the temperature

to rise to any appreciable extent.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 187–188.

Lyons, A. B., points out that the omission of the word “pure,” in connection with the assay requirement for the compound solution of iodine, does not coincide with the purity statement under iodine.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 261.

Kleinschmidt, A. A., points out that the tincture of iodine, U. S. P., VIII, is a compound, not a simple tincture, and should be so labeled.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 404.

Williams, John K., thinks that the U. S. P., VIII, directions to triturate the ingredients in making tincture of iodine entail an absurd waste of time. He prefers to put the ingredients into a shop bottle and shake occasionally.—*Proc. Connecticut Pharm. Ass.*, 1905, p. 51.

Caldwell, Paul, recommends making tincture of iodine by circulatory displacement, using cheese cloth or gauze to hold the iodine.—*Drug Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 220.

Remington, J. P., justifies the addition of potassium iodide to the tincture of iodine in the U. S. P., VIII, on the ground that it acts as a preservative, prevents the loss of free iodine, and will thus obviate the prosecution of pharmacists for selling tincture of iodine deficient in strength.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 254.

Dohme, A. R. L., examined 4 samples of tincture of iodine which varied from 1.2 to 7.1 per cent of free iodine. Two of the samples, containing less than 3 per cent of iodine each, were evidently diluted with water and were thoroughly bad.—*Proc. Maryland Pharm. Ass.*, 1905, p. 49.

LaWall, Charles H., reports on 8 samples of tincture of iodine which varied from 7.74 to 1.4 per cent of free iodine; 4 of the samples contained less than 3 per cent, and 2 additional samples less than 4 per cent of free iodine. One sample was made with wood alcohol.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 185.

Blanchi, A., discusses the preparation of iodine ointment and proposes the use of iodine oleate as a basis. This oleate may be prepared by pouring an alcoholic solution of 1 part of iodine into 3 parts of oleic acid and evaporating the alcohol at a low temperature.—*Boll. Chim. Farm.*, Milano, 1905, v. 44, pp. 553–558.

Kinnaman, Guy C., presents the results of a comprehensive investigation on the action of the more important antiseptic substances containing iodine in chemical combination.—*J. Am. M. Ass.*, Chicago, 1905, v. 45, p. 601.

Schürhoff, P., reports experiments made with iodine combinations to determine their decomposition in the animal organism.—*Arch. internat. de Pharmacod. et de Thérap.*, 1905, v. 14, pp. 429–436.

Nigoul, M., presents a comparative study of the action of tincture of iodine, potassium iodide, and iodosol, the latter a name given to a

preparation similar to or identical with a 6 per cent solution of iodine in saponated petrolatum N. F. (1906).—*Progrès Méd.*, Paris, 1905, v. 21, pp. 849–852.

Wesenberg, G., discusses the percutaneous application of iodine (*Therap. Monatsch.*, Berlin, 1905, v. 19, pp. 199–207).—Reference from *Ind. Med.*, 1905, p. 460.

Witzel, A., reports a case of acute poisoning of the mucous membrane of the mouth by local application of tincture of iodine (*Deutsch. Med. Wehnschr.*, 1905, v. 31, p. 1839).—*Ibid.*, p. 110.

IODOLUM.

An editorial says of iodol:

A surprising addition. Was never popular, and has long since been discarded by surgeons in favor of other iodine compounds.—*Drug Topics*, 1905, v. 20, p. 197.

IPECACUANHA.

Lloyd, John Uri, asserts that ipecac is likely to be of inferior quality, and is not infrequently admixed with other foreign drugs.—*Pharm. Rev.*, 1905, v. 23, p. 330.

An editorial discusses the admission of Carthagena ipecac into the U. S. P., VIII, and points out that pharmaceutical chemists have demonstrated that the two roots are not identical.—*Drug Circ. & Chem. Gaz.*, 1905, v. 49, p. 343.

An editorial expresses the opinion that the recognition of both the Rio and Carthagena variety of ipecac serves to show the inconsistency of man, and points out that the proportion of the alkaloids in the two drugs is widely divergent.—*Drug Topics*, 1905, v. 20, p. 214.

Dohme, A. R. L., believes that ipecac is used principally for emetic purposes, and that therefore the Carthagena root is preferable to the Rio in every way.—*Apothecary*, Boston, 1905, v. 17, p. 942.

Moore, Russell W., in discussing the quality of drugs coming into the port of New York, points out that while formerly Carthagena ipecac was excluded as spurious, it is now admitted, provided it contains 1.8 per cent of alkaloids. Of 204 samples examined, 10 were below this standard.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 266.

Gehe & Co. point out that the former marked difference in price between Rio and the Carthagena varieties of ipecac has been nearly equalized by the increased demand for the latter root.—*Gehe & Co., Handels-Ber.*, 1905, p. 43.

Braun, K., discusses the botany, chemistry, and the cultivation of ipecac and makes some comment on the available varieties to be selected for cultivation and the best methods of collecting and treating the drug.—*Der Pflanzer*, Tanga, 1905, v. 1, pp. 50–53.

Hartwich, C. (Arch. d. Pharm., v. 242, p. 647), discusses the identification of ipecac and some of its substitutes by means of the structural characteristics shown under the microscope.—Abstr. in Proc. Am. Pharm. Ass., 1905, v. 53, p. 640.

Collin, Eug., points out that for the recognition of the several varieties of ipecac the determination of the size of the starch granules and of the crystals that are present offers a ready method for differentiating between them.—Just's Bot. Jahresber. for 1905, v. 33, part 3, p. 198 (from J. de Pharm. et de Chim., v. 20, pp. 293-300).

Mannich and Brandt (J. de Pharm. et de Chim., v. 20, p. 276) report the root of *Heteropteris pauciflora*, mentioned by Peckolt of Rio, as being used to adulterate ipecac. While in external appearance this root closely resembles ipecac, its histological structure is markedly different. It contains no starch or raphides of calcium oxalate but shows cells containing a peculiar brown coloring matter.—Analyst, Lond., 1905, v. 30, p. 60.

Vanderkleed, Charles E., reports 14 assays of ipecac which varied from 2.01 to 2.63 per cent of ether-soluble alkaloids. The general quality of this drug he believes to be very good.—Proc. Pennsylvania Pharm. Ass., 1905, p. 56.

An abstract asserts that during the past year comparatively little ipecac was found that complied with the Ph. Germ., IV, requirement of 2.03 per cent of alkaloid. Of 19 samples examined only 3 were found to comply with this requirement.—Suedd. Apoth. Ztg., 1905, v. 45, p. 528.

Stanislaus, I. V. S., offers some remarks on the ipecac root of the pharmacopœia.—Am. Druggist, N. Y., v. 47, p. 350.

Maben, Thomas, believes that the reduction of the standard to 1.75 per cent of alkaloids is a mistake. It seems unwise to reduce the standard to what is practically the lowest strength found in commerce.—Pharm. J., Lond., 1905, v. 21, p. 141.

Caeser and Loretz outline a method for the assay of ipecac in which they recommend ether as the primary solvent in place of the ether chloroform mixture directed by the U. S. P., VIII.—Geschäfts-Ber. von Caeser & Loretz, in Halle a. S., 1905, p. 93.

Gadd and Gadd point out the necessity for examining preparations of ipecac because of the doubt that has been cast upon the stability particularly of the liquid preparations.—Pharm. J., Lond., 1905, v. 21, p. 439.

Naylor, W. A. H., discusses the standardization of the galenical preparations of ipecac and the several methods of assay that have been proposed.—*Ibid.*, p. 124.

Lyons, A. B., believes that the official fluid extract of ipecac will find no favor with pharmacists because it is loaded with resinous

matter, and so can not be mixed directly with syrup to make the official syrup of ipecac.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 258.

JALAPA.

Eberle, E. G., says that *Jatropha macrorhiza* has a large globular rhizome having emetic and purgative properties. It is kept in drug stores along the Mexican border and is known as jalapa.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 306.

Maben, Thomas, points out that the curious fall in the resin content of jalap has been experienced in the United States as well as in England, and the U. S. P., VIII, standard has been modified accordingly. As Umney has pointed out, pharmacopœial standards have varied from 18 to 7 per cent.—Pharm. J., Lond., 1905, v. 21, p. 141.

Vanderkleed, Charles E., reports assays of jalap which varied from 0.48 to 8.2 per cent of resin. The general quality of this drug he asserts is poor.—Proc. Pennsylvania Pharm. Ass., 1905, v. 56.

Dohme, A. R. L., asserts that jalap root is getting poorer and poorer, and it is now almost impossible to get any jalap root that will pass the U. S. P. standard. The laboratory report indicates that the quality has decreased steadily from 1899, when the average resin content was 11.21 per cent, to 1905, when the average is but 6.2 per cent.—Apothecary, Boston, 1905, v. 17, p. 942.

Gane, E. H., reports on 1,000 pounds of jalap, which yielded an average of 8 per cent of resin.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 185.

Gehe & Co. report that the bulk of the available jalap in the spring of 1905 consists of small immature tubers containing barely 7 per cent of resin.—Gehe & Co., Handels-Ber., 1905, p. 50.

Moore, Russell W., believes that the lowering of the standard in the U. S. P., VIII, appears to be fully justified by the condition of the market. He reports the average resin content of the drug examined in 1904 and since that time, and ventures the suggestion that evidently little care is exercised by the gatherers of this drug.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 266.

Caeser and Loretz recommend extracting the powder with absolute alcohol, heated in connection with a reflux condenser. An aliquot part of the resulting solution is partially evaporated and then treated with water. The resulting resin is dried and weighed.—Pharm. Ztg., Berlin, 1905, v. 50, p. 773.

Gadd and Gadd outline a method for determining the extractive present in tincture of jalap.—Pharm. J., Lond., 1905, v. 21, p. 439.

KAOLINUM.

Schimpf, Henry W., commends the inclusion of kaolin in the U. S. P., VIII, and points out some of the uses to which it may be put.—Am. J. Pharm., 1905, v. 77, p. 516.

KINO.

Hooper, David, reports on a kino obtained from *Croton tiglium*.—Pharm. J., Lond., 1905, v. 21, p. 479.

KRAMERIA.

Eberle, E. G., points out that *K. parvifolia*, *ramosissima*, *canescens*, and *secundiflora* grow in Texas and that the latter seems to be equal to the official krameria in medicinal properties and in tannin content.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 306.

LACTUCARIUM.

Kieffer, G., describes the cultivation of *Lactuca virosa* as carried on in the valley of the Mosel and the production of lactucarium. It is further asserted that the greater portion of the resulting drug is exported to England and from there to America, particularly to San Francisco, where it is supposedly used for the adulteration of opium.—Pharm. Ztg., 1905, v. 50, p. 143.

An unsigned article discusses the several varieties of lactucarium designated as German, French, English, Russian, and Canadian, and presents some facts as to their origin and composition.—Nouv. Rem., 1905, v. 21, pp. 137-138.

The revisors of Vienna pharmacies report finding lactucarium that was adulterated with bread dough.—Pharm. Prax., 1905, v. 4, p. 38.

LIMONIS CORTEX.

Patch, Edgar L., found four samples of extract of lemon which contained over 40 per cent of wood alcohol.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 184.

Thurston, Azor, found great variation in the extract of lemon sold, only two of a number of samples examined complying with the U. S. P. requirements.—Proc. Ohio Pharm. Ass., 1905, p. 35.

LIMONIS SUCCUS.

The Jahresbericht des Berner Kantonchemikers points out that the literature on the composition of lemon juice is meagre, the most comprehensive publication being that by Ed. Spaeth (Ztschr. f. Unters. d. Nahr. u. Genussm., 1901, p. 529). The experiments made at Bern with eight samples of lemon juice indicate a variation of from 6.02 to 9.24 gm. of citric acid in each 100 cc. of lemon juice. The ash varied from 0.20 to 0.52 gm. in each 100 cc., the alkalinity of the resulting ash requiring from 2 to 5.6 cc. of normal alkali.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 456.

LINIMENTA.

Sayre, L. E., suggests that if a maximum and a minimum requirement for moisture in granulated soap were made, it would insure a more uniform soap liniment. As it is, he believes that this preparation frequently gives trouble.—*Pharm. Era*, 1905, v. 34, p. 197.

Havenhill, L. D., points out that there is a wide variance in the composition of "castile" soaps, and that they do not all comply strictly with the requirements of the U. S. P. He recommends the use of the best available castile soap, in bars, and preparing the powder or dry granulation from this.—*Proc. Kansas Pharm. Ass.*, 1905, pp. 77-79.

Schaumann recommends preparing the liniment of soft soap (*Spiritus Saponatus*, *Ph. Germ.*, IV) directly from the olive oil and alkali, and outlines a process with formula.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 814.

Caldwell, Paul, asserts that if the liniment of turpentine is to remain in a liquid state equal parts of rosin cerate and oil of turpentine should be used in making it instead of 650 and 350 gms., respectively, as now directed.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 306.

LINUM.

Wetterstroem, T., reports that personally ground flaxseed gave 34.2 per cent of oil, while samples of ground flaxseed bought in the open market gave from 21.8 to 25.7 per cent of oil.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 185.

Bigelow, Edward P., examined 12 samples of ground flaxseed, of which 3 were adulterated, 4 samples showed a low specific gravity, and 3 showed a strong fluorescence; 2 samples were below the required yield of pure oil.—*Proc. Massachusetts Pharm. Ass.*, 1905, p. 103.

Mittelbach, Wm., for keeping flaxseed free from bugs recommends storing in a tin can, with close-fitting top, and keeping in the bottom of this can a small vial, loosely stoppered, containing chloroform.—*Pharm. Era*, N. Y., 1905, v. 34, p. 388.

LIQUOR ANTISEPTICUS.

Nixon, C. F., believes that the official antiseptic solution will not prove of much use, as it is not a desirable preparation.—*Apothecary*, Boston, 1905, v. 17, p. 774.

An editorial ventures the opinion that—

It does not appear that the pharmacopœia is just the place for what are really toilet and not medicinal articles.—*Drug Topics*, 1905, v. 20, p. 197.

Thornton, E. Q., expresses the opinion that antiseptic solution is, strictly speaking, a toilet article.—*Therap. Gaz.*, 1905, v. 29, p. 737.

LIQUOR CALCIS.

Ilhardt, W. K., found a sample of limewater containing but 0.098 per cent of calcium hydrate.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 184.

The committee on adulteration reports collecting samples of lime-water in the city of Detroit which were not up to the official standard.—*Proc. Michigan Pharm. Ass.*, 1905, p. 80.

Caldwell, Paul, recommends the use of a barrel, with a wooden spigot or a glass siphon, for making limewater.—*Drug. Circ. & Chem. Gaz.*, 1905, p. 220.

Pritchard, B. E., recommends the use of an inverted 5-gallon bottle, with provision made for air and a tube running well into the neck of the bottle so as to allow the superfluous lime to settle in the neck below the opening of the tube.—*Am. Druggist*, N. Y., 1905, v. 47, p. 3.

LIQUOR CHLORI COMPOSITUS.

Davidson, E., discusses the chemical reactions that are involved in the decomposition of potassium chlorate by means of hydrochloric acid.—*Ztschr. f. angew. Chem.*, 1905, v. 18, pp. 1047-1054.

LIQUOR CRESOLIS COMPOSITUS.

Schumacher, R. (*Ztschr. f. angew. Chem.*, v. 18, p. 1361), asserts that the *Liquor cresoli saponatus* of the *Ph. Germ.*, IV, has frequently been found to contain, in place of cresol, crude carbolic acid.—*Abstr. in Merck's Rep.*, N. Y., 1905, v. 14, p. 347.

LIQUOR FERRI ET AMMONII ACETATIS.

Fisk, Frank E., suggests preparing the solution of iron and ammonium acetate extemporaneously, using glacial acetic acid in place of the diluted acetic acid directed in the official formula for making solution of ammonium acetate.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 394.

LIQUOR FORMALDEHYDI.

Auerbach and Barschall present a comprehensive study of the nature and composition of aqueous solutions of formaldehyde, including a review of the work previously recorded, a full description of methods of analysis, the determination of the various constants and the consideration of the several theories that have been advanced regarding solutions of formaldehyde.—*Arb. a. d. Kais. Gesundheits-amte*, 1905, v. 22, p. 584.

Morel, A., describes and figures the apparatus and the process used for the production of solutions of formaldehyde at the French works

of the Cote d'Or.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 289 (from *J. de Pharm. et de Chim.*, 1905, v. 21, pp. 177–183).

Chapman and Holt have succeeded in producing a synthetic formaldehyde from a mixture of carbon monoxide, hydrogen, and steam.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 792 (from *Chem. Soc. Trans.*, 1905, v. 87, pp. 916–921).

Goldschmidt, Carl, points out that formaldehyde in solution exists as a hydrate of methyleneglycol. While commercial solutions ordinarily contain from 36 to 40 per cent of formaldehyde, it is possible to absorb as much as 50 per cent.—*Pharm. Zentrall.*, 1905, v. 46, p. 643.

Wetterstroem, T., examined 11 samples of solution of formaldehyde which ranged from 29 to 37 per cent by weight, 30.8 to 39.8 per cent by volume. Three of the samples were below 37 per cent.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 184.

Smith, Bernard H., discusses the methods used in the analysis of formaldehyde, the results that were obtained, and includes a table of the percentage strength of commercial formaldehyde samples obtained in 1905.—*Proc. Ass. Off. Agr. Chem.*, 22 Ann. Conv. (1905), 1906, pp. 29–31.

Williams, R. H., presents a comparative study of the several methods used for the determination of formaldehyde. He concludes that the iodometric estimation is rapid and accurate and preferable for dilute solutions. The hydrogen peroxide method is the most satisfactory for strong impure solutions, though the time necessary for complete oxidation is widely variable, depending on concentration and temperature. The potassium cyanide method is recommended for dilute, impure solutions. The end point in the Legler method is not considered satisfactory.—*J. Am. Chem. Soc.*, v. 27, pp. 596–601.

Fresenius and Grünhut discuss the applicability of several widely used methods of analysis and present slight modifications for the peroxide method and the iodometric method.—*Ztschr. f. analyt. Chem.*, 1905, v. 44, pp. 13–24.

Haywood and Smith present a study of the hydrogen peroxide method for determining formaldehyde. They discuss the methods that have been proposed by Blank and Finkbeiner and by Fresenius and Grünhut and suggest a modification of the former.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 1183–1188.

La Wall, Charles H., presents a comparative study of the tests for formaldehyde, with results obtained, and expresses himself as being unhesitatingly in favor of the phenylhydrazine test, both on account of its simplicity and the decided reactions obtained in all of the dilutions with which experiments were made. He thinks that the delicacy of some of the tests, such as the phenol-sulphuric acid test

and the resorcinol-sulphuric acid test, has been exaggerated.—*Proc. N. J. Pharm. Ass.*, 1905, pp. 67-73.

Bonnet, Frederic, jr., describes a test for formaldehyde with a sulphuric acid solution of morphine.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 601-605.

Frankforter and West outline a method for the gasometric determination of formaldehyde, which depends on the liberation of hydrogen from a mixture of formaldehyde, caustic alkali, and hydrogen peroxide.—*Ibid.*, pp. 714-719.

Lyons, A. B., proposes a modification of Hehner's test so as to make it applicable for the detection of formaldehyde in liquids other than milk. The test depends on the presence of proteids, which he proposes to introduce in the form of beef peptone. He asserts that the test will show the presence of 1:4000000 parts of formaldehyde.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 326-329.

Lindet (*Apoth. Ztg.*) proposes the use of casein, dilute ferric chloride solution, concentrated phosphoric and sulphuric acids for detecting formaldehyde in alcohol.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 390.

Puckner, W. A., discusses the U. S. P., VIII, test for formaldehyde in witch hazel extract, and concludes that the official test when properly applied will show the presence of 1 gm. of formaldehyde in 10000 cc. of a 15 per cent alcohol solution. To avoid possible failure he suggests that the test be made to read:

If 1 cc. of hamamelis water be added to 5 cc. of a freshly prepared solution of 0.01 gm. of salicylic acid in 100 cc. of sulphuric acid, no red color should appear on standing (absence of formaldehyde).—*Am. J. Pharm.*, Phila., 1905, v. 77, p. 501.

Mörner, Carl Th., discusses the use of formaldehyde solution as a reagent.—*Svensk. Farm. Tidskr.*, 1905, v. 9, pp. 303-304.

Lyons, A. B., suggests the use of formaldehyde as a reagent for sugars, and also for morphine and codeine.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 329-332.

Walker, Henry V., reviews the methods used for generating formaldehyde gas for fumigating purposes, and outlines a new method which depends on the use of formaldehyde solution, aluminum sulphate, and lime.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 277-278.

Goldschmidt, Carl, reviews the literature bearing on disinfection by means of formaldehyde.—*Pharm. Zentralh.*, 1905, v. 46, p. 651.

Rosenberg, P., discusses the value of formaldehyde for internal therapy, and also reviews the literature relating to the internal use of this drug.—*Therap. d. Gegenw.*, 1905, v. 7, pp. 55-62.

Hart, J. I., discusses the use of formaldehyde solution for hardening dental pulp.—*Dental Cosmos*, 1905, v. 47, p. 563.

See also Ewald, E. H. (from Dental Summary, 1905).—*Ibid.*, p. 627.

LIQUOR MAGNESII CITRATIS.

The committee on adulteration found 2 samples, out of 32, that were solutions of sodium citro-tartrate, the rest were found to be as labeled.—Proc. Louisiana Pharm. Ass., 1905, p. 44.

Persse, Jefferson D., believes that the addition of tartaric acid would materially improve the official formula for solution of magnesium citrate.—Proc. Georgia Pharm. Ass., 1905, p. 75.

Archetti, Andrea, proposes a modification for the official (Italian) process for making "Limonata Magnesica," a preparation similar to the liquor magnesii citratis.—Boll. Chim. Farm., 1905, v. 44, pp. 449-451.

Hain, Frank W. A., asserts that he has no trouble in keeping solution of magnesium citrate from spoiling, if it is kept in the ice box.—Bull. Pharm., Detroit, 1905, v. 19, p. 472.

LIQUOR PLUMBI SUBACETATIS.

Merson, G. F., discusses the method of preparing strong solution of lead subacetate and expresses his preference for a gravimetric process of estimating the lead content.—Year Book of Pharmacy, 1905, p. 266 (from Pharm. J., Lond., v. 20, p. 70.)

LIQUOR POTASSII ARSENITIS.

Pascal (from Bull. commerc., 1905, No. 10) believes that the presence of alcohol in solution of potassium arsenite is the disturbing factor and the cause of the flocculent precipitate so frequently met with. He proposes the use of distilled melissa water in place of the spirit of lavender and water so widely used.—Pharm. Ztg., Berlin, 1905, v. 50, p. 1009.

LITHII CARBONAS.

Geffcken, Gustav, points out that lithium carbonate, which is but slightly soluble in water, dissolves more readily in solutions of the alkali salts, the sulphates of ammonium, sodium, and potassium exercising a greater influence than the corresponding chlorides. The author includes a table and a chart to illustrate the variability with solutions of various concentrations.—Ztschr. f. anorgan. Chem., 1905, v. 43, pp. 197-201.

Herrmann, E. (from Pflüg. Arch. d. Physiol, 1905), has been able to demonstrate that lithium is actually present in the human body as an integral part of even the foetus, and that it no doubt has some physiologic significance.—Pharm. Ztg., Berlin, 1905, v. 50, p. 927.

LITHII CITRAS.

Dott, D. B., points out the inaccuracy of the Ph. Brit., IV, description of lithium citrate, and records finding 24.7 per cent of water of

crystallization in place of 19 per cent as described.—Abstr. in Proc. Am. Phar. Ass., 1905, v. 53, p. 804 (from Pharm. J., London, 1905).

LOBELIA.

Lloyd, John Uri, points out that lobelia is likely to be contaminated with other herbaceous plants. The seed, he asserts, has been in some cases altogether substituted by the seed of mullein which, to the eye, it very nearly resembles, the compound microscope being necessary to differentiate between them.—Pharm. Rev., 1905, v. 23, p. 331.

True, Rodney H., reports that *Lobelia inflata* is grown regularly in the testing gardens of the Bureau of Plant Industry of the U. S. Dept. of Agriculture.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 275.

The Bureau of Plant Industry suggests planting the seed of lobelia in the autumn.—Ann. Rep. U. S. Dept. Agric., 1905, p. 147.

Havenhill, L. D., found one sample of powdered lobelia which contained 9.3 per cent of moisture and 12.6 per cent of ash. Nearly one-half, or 5.8 per cent, of the ash was sand.—Proc. Kansas Pharm. Ass., 1905, p. 92.

Vanderkleed, Charles E., reports 3 assays of lobelia, which varied from 0.72 to 1.48 per cent of alkaloid, the average standard for good drug being 5.0 per cent.—Proc. Pennsylvania Pharm. Ass., 1905, p. 56.

An editorial points out that while the change from hydro-alcoholic to an acetic acid menstruum may be of advantage in connection with the fluid extract of squill and the fluid extract of sanguinaria, the change is doubtful in connection with fluid extract of lobelia.—Drug Topics, 1905, v. 20, p. 194.

LUPULINUM.

Moore, Russell W., points out that the indirect method of determining the quality of lupulin by means of the ash was held to be less satisfactory than a direct estimation of the valuable or ether soluble portion. Of 25 samples examined only 2 contained less than the standard of 10 per cent of ash, while 12 were above the minimum of 70 per cent of ether extract. The ash allowance of the Ph. Brit., IV, 15 per cent, appears to be entirely compatible with the 70 per cent of ether extract of the U. S. P., VIII.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 267.

The revisors of Vienna pharmacies found lupulin which contained from 7.42 to 28.22 per cent of ash and point out that an ash content of more than 10 per cent is objectionable.—Pharm. Prax., 1905, v. 4, p. 38.

LYCOPODIUM.

Caeser and Loretz point out that while the Ph. Germ., IV, allows 5 per cent of ash, this allowance contradicts the other requirements. Pure lycopodium has less than 1 per cent of ash, and any excess would be due to foreign admixture. They also point out that the accidental admixture of pollen grains, or even the occasional appearance of starch grains, should not suffice to condemn lycopodium.—Geschäfts-Ber. v. Caeser & Loretz, in Halle a. S., 1905, p. 9.

The revisors of Vienna pharmacies found lycopodium which was adulterated with pine pollen, "*Lycopodium Hungaricum*," talcum, and starch.—Pharm. Prax., 1905, v. 4, p. 38.

Havenhill, L. D., reports that of 17 samples examined none showed the presence of impurity in suspicious amounts.—Proc. Kansas Pharm. Ass., 1905, p. 92.

van Itallie, L., discusses several adulterants of lycopodium, and calls particular attention to powdered amber as a substitute for lycopodium.—Pharm. Weekbl., 1905, v. 42, pp. 189-190.

Geiser, S. R., asserts that lycopodium is valuable in mental depression, katatonic dementia, gravel, and chronic constipation.—Trans. Am. Inst. Homœop., 1905 p. 355.

MAGNESII CARBONAS.

Patch, Edgar L., reports finding from 44 to 51 per cent of carbonate and traces of calcium.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 185.

"Gnomon" points out that in many places the public expect the carbonate when they ask for "magnesia," though the name properly applies only to the oxide.—Pharm. J., Lond., 1905, v. 21, p. 480.

MAGNESII SULPHAS.

Meltzer and Auer report a series of experiments made to determine the anæsthetic properties of magnesium salts. They conclude that a certain dose of magnesium sulphate will produce a lasting anæsthesia with complete relaxation of all the voluntary muscles and abolition of some of the less important reflexes.—Am. J. Physiol., 1905, v. 14, pp. 366-388.

An editorial comments on the work done by Meltzer and Auer on the use of magnesium sulphate as a general anæsthetic.—J. Am. M. Ass., 1905, v. 45, p. 1959.

Gregory, E. B., suggests masking the taste of magnesium sulphate by triturating with saccharin and bicarbonate of soda and adding tartaric acid.—Eclectic Med. J., 1905, v. 65, p. 429.

MALTUM.

Trillich, Heinrich, discusses the nature and identity of malt, and gives a definition which provides that this substance is the artificially germinated grain whose growth has progressed sufficiently to cause the contained ferment to change the available starch to malt dextrin and sugar.—*Ztschr. f. oeffentl. Chem.*, 1905, v. 11, pp. 259–261.

MANGANI DIOXIDUM PRÆCIPITATUM.

Kebler, Lyman F., reports finding a 70 per cent pure manganese dioxide which contained sodium chloride, calcium, and magnesium.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 185.

Gröger, Max, outlines a modification of the method devised by Volhard for determining a manganese in the presence of chromium. In place of zinc oxide or zinc hydroxide he uses a mixture of basic zinc sulphate with a solution of normal zinc sulphate.—*Chem. Ztg.*, Cöthen, 1905, v. 29, p. 987.

Schlagdenhauffen and Reeb report an extensive investigation on the presence of manganese in various animal and vegetable substances.—*J. de Pharm. v. Elsass-Lothr.*, 1905, v. 32, pp. 47–61, 80–89, and 114–120.

MARRUBIUM.

Eberle, E. G., mentions *Marrubium vulgare* in his list of medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 304.

MASSA HYDRARGYRI.

Lowe, Clement B., asserts that the U. S. P. formula for mass of mercury is satisfactory. He overcomes the tendency to drying by placing a common school sponge, slightly moistened with water, in the jar for six or eight hours.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 138.

MATICO.

Thoms, H., discusses the origin, variability, and uses of matico oil and includes a report of an investigation into the chemistry of the substance. In a second communication he discusses the composition of matico oil and the chemistry of its constituents.—*Arb. a. d. Pharm. Inst. d. Univer., Berlin*, 1905, v. 2, pp. 100–115 and 120–126.

MATRICARIA.

Eberle, E. G., mentions *Matricaria chamomilla* among the medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 304.

MEL.

An abstract from the Helfenberger Annalen points out that the test for dextrin, as given in the *Ph. Germ.*, IV, is too delicate, and

should be more fully defined so as to direct the gradual addition of the alcohol, or to modify the test entirely.—Pharm. Ztg., Berlin, 1905, v. 50, p. 672.

Stadlinger, Hermann, presents a comprehensive article on the examination of honey: chemical, physical, and microscopical.—Pharm. Ztg., Berlin, 1905, v. 50, pp. 536 and 549.

An abstract discusses the suggestion made by Herm. Ley to dilute the honey that is to be purified, adding a small proportion of alcohol and sufficient lime water to make the solution neutral or slightly alkaline. After filtering the solution may be treated with oxalic acid to remove the lime, again filtered and then concentrated to the proper consistency.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 23.

Kühn, W., reviews the general subject of poisonous honeys, and refers particularly to a study of cases, happening in New Zealand, reported by Auben in the British Medical Journal.—Pharm. Ztg., Berlin, 1905, v. 50, p. 640.

MENTHA PIPERITA.

Eberle, E. G., mentions *Mentha piperita* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, p. 304.

Todd, A. M. (Proc. Int. Kongr. angew. Chem., pp. 804–812, 1903, Ber. 2), gives a brief historical account of the peppermint industry since it began in England in 1750; also some account of the large mint farms in Michigan and of methods of distillation.—Exp. Sta. Rec., 1906, v. 17, p. 766.

Henkel, Alice, discusses the cultivation of peppermint in the United States, including some reference to the history and a detailed description of the three kinds of mint grown for the production of peppermint oil: *Mentha piperita*, L.: *Mentha piperita vulgaris*, Sole, and *Mentha piperita officinalis*, Sole.—Bul. Bur. Plant Ind., U. S. Dept. Agric., No. 90, 1906, 8vo.

The revisors of Vienna pharmacies (from Ztschr. d. oesterr. Apoth. Ver.) report *Mentha piperita* frequently contaminated with the leaves of *Mentha viridis*, and in one instance the leaves of *Atropa belladonna*. The latter admixture, they point out, while no doubt accidental, is sufficient to indicate the care that should be exercised in the selection of crude drugs of all kinds.—Pharm. Prax., 1905, v. 4, p. 38.

Vanderkleed, Charles E., recommends the use of 10 per cent solution of sodium chloride for washing the acetylated oil in the determination of menthol.—Proc. Pennsylvania Pharm. Ass., 1905, p. 193.

MENTHA VIRIDIS.

Lloyd, John Uri, asserts that little care is exercised to separate spearmint from its relative peppermint, and, as they naturally grow

in the same situations, contamination of the one with the other is common.—Pharm. Rev., 1905, v. 23, p. 331.

Eberle, E. G., mentions *Mentha viridis* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

MENTHOL.

Siedler, P., believes that the Ph. Germ., IV, melting point requirement for menthol (43°) is low; he found it to require 44.5° C.—Pharm. Post, Wien, 1905, v. 38, p. 568.

The experiments recorded by Riedel indicate that the boiling point of menthol is approximately 216.65° at ordinary barometric pressures, or about 4.65° higher than the boiling point given in the Ph. Germ., IV, and in the U. S. P., VIII.—Riedel's Berichte, Berlin, 1905, p. 46.

Zederbaum, George, discusses the treatment of sensitive dentine in shallow cavities by the use of menthol.—Dental Cosmos, Phila., 1905, v. 47, p. 151.

MENTHYLIS SALICYLAS.

Wetterstroem, Theo. D., quotes a large jobber as saying that the substitution of synthetic for natural oil of wintergreen "is the most profitable side line in his business."—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 312.

MORPHINA.

The Bureau of Plant Industry reports the perfecting, on a laboratory scale, of a method for the extraction of a very high grade of crude morphine from the dried tissues of the poppy plant capsule.—Ann. Rep. Dept. Agric., 1905, p. 149.

Firbas, Richard, has studied the action of acacia on morphine, and believes that acacia in solution tends to change morphine into oxy-morphine. The latter when present in any appreciable quantity, may be detected by the use of potassium dichromate.—Apoth. Ztg., Berlin, 1905, v. 20, p. 1031.

Reichard, C. (Chem. Ztg., v. 28, p. 1182), reviews the several tests and reactions for morphine.—Pharm. Prax., 1905, v. 4, p. 309.

An abstract (from Pharm. Zentrallh., 1905) points out that both morphine and codeine give the same color with sulphuric acid and formaldehyde. With sulphuric acid and chloral or bromal, however, morphine gives a violet, while codeine yields a blue-gray color. When both alkaloids are present in a sample, the color is brown-violet.—Apothecary, Boston, 1905, v. 17, p. 628.

"Sz" reviews the work that has been done on the constitution of morphine, codeine, and thebaine.—Pharm. Zentrallh., 1905, v. 46, p. 907.

Pschorr and Knorr (from Med. Klin., 1905, p. 870) report researches made on the composition of morphine and some of its derivatives.—Apoth. Ztg., Berlin, 1905, v. 20, p. 629.

Halle, Walter L., presents a didactic paper outlining the history of morphine and some account of the evolution of our knowledge regarding the composition and chemistry thereof.—Chem. Ztg., Cöthen, 1905, v. 29, p. 1264.

Kebler, Lyman F., found morphine tablets which differed widely from the labeled strength; some also contained cane sugar instead of milk sugar, as labeled.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 185.

Gérard, Deléard, and Ricquet review the work done on the toxicologic detection of morphine, and report on experiments made to demonstrate why some investigators have been able to detect only oxymorphone.—J. de Pharm. et de Chim., Paris, 1905, v. 22, p. 49.

Babel, Alex., reports a study on the behavior of morphine, codeine, dionin, and heroin in the animal organism.—Arch. f. exper. Path. u. Pharmakol., Leipzig, 1905, v. 52, pp. 262–270.

Hausmann, Walter, reports experiments made in connection with the study of tolerance to morphine in man and some of the higher animals.—*Ibid.*, pp. 315–325.

Luzzatto, Riccardo, reports observations made to determine the cause of glycosuria in cases of poisoning by morphine.—*Ibid.*, pp. 95–106.

Foderá, F. A., discusses the memoir of De Busscher on the use of permanganate as an antidote for morphine.—Arch. Internat. de Pharmacol. et de Thérap., 1905, v. 14, pp. 273–301.

MYRRHA.

Tschirch and Bergmann discuss the probable origin of the official myrrh, and suggest that until the origin of this drug can be definitely determined it would be preferable to specify that “it is derived from a variety of *Commiphora* indigenous to northeast Africa.” They also present an account of experimental work done with a sample of myrrh of known origin.—Arch. d. Pharm., 1905, v. 243, p. 641.

Alcock, F. H., found from 3.8 to 17 per cent of ash in commercial myrrh; he also found that a considerable proportion of this ash was composed of magnesium, and proposes that this high percentage of magnesium may serve as a control for adulterations.—Apoth. Ztg., Berlin, 1905, v. 20, p. 671.

The revisors of Vienna pharmacies found myrrh adulterated with Bdellium and Bissabol myrrh.—Pharm. Prax., 1905, v. 4, p. 38.

Peters, E. J. (Wiener illustrierte Gartenzeitung, 1905, pp. 34–36), presents a review of the plants producing myrrh and some reference to their cultivation.—Bot. Centralbl., 1905, v. 100, p. 93.

MYRISTICA.

Spaeth, E., believes that the microscopic structure of mace should be considered. Powdered nutmegs frequently consist of inferior or damaged kernels. Commercially satisfactory nutmeg should consist of the undamaged drug. The ash of the air dry drug should not exceed 3.5 per cent and the portion insoluble in 10 per cent hydrochloric acid should not exceed 0.5 per cent.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, 1905, v. 10, p. 26.

Just's *Botanischer Jahresbericht* (1905, v. 33, part 3, p. 752) contains several references to the cultivation of nutmeg.

NAPHTHALENUM.

Riedel's *Berichte* asserts that the Ph. Germ. requirement, 218° , was found to correspond fairly well with the boiling point of an approved sample of naphthalene, at a pressure of 760 mm. With a variation of from 720 to 790 mm. pressure, the boiling point varied from 215.7 to 220.1° C.—*Riedel's Berichte*, Berlin, 1905, p. 47.

NUX VOMICA.

Dohme, A. R. L., points out that nux vomica has run pretty uniformly, about 2.5 per cent total alkaloids, or about 1.25 per cent strychnine, the maximum variation during the seven years 1899 to 1905 being 2.3 per cent in 1899 to 2.9 per cent in 1903.—*Apothecary*, Boston, 1905, v. 17, p. 942.

Vanderkleed, Charles E., reports 5 assays for nux vomica, which varied from 2 to 2.9 per cent of total alkaloids.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 56.

Philip Röder reports the examination of 7 samples of nux vomica, which varied from 9.59 to 11.83 per cent of water, and from 1.15 to 2.91 per cent of ash. Three samples that were assayed yielded from 3.44 to 5.31 per cent of total alkaloids.—*Pharm. Post*, Wien, 1905, v. 38, p. 392.

Gadd, Sydney C., contributes some laboratory notes on nux vomica seeds, the determination of the reaction of the fat present, and some additional data on the liquid extract and commercial samples of tincture.—*Pharm. J., Lond.*, 1905, v. 21, p. 134.

Harvey and Wilkie have examined the fat obtained by extracting the seeds of nux vomica with ether. A high content of unsaponifiable material appears to be characteristic of nux vomica. The free acid present ranges from 56.7 to 6.9 per cent, calculated as oleic.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 718-719.

Naylor, W. A. H., discusses the several processes suggested for the assay of nux vomica and concludes that a satisfactory and expedi-

tious process for the assay of nux vomica could easily be devised by adopting either Alcock's or Bird's method of extracting and purifying the mixed alkaloids and subsequently separating the strychnine by nitric acid as described by Dowzard.—*Pharm. J., Lond.*, 1905, v. 21, p. 125.

Howard, D. Lloyd, presents a note on the separation of strychnine and brucine. He discusses Keller's method and Gordin's modification of that method, and concludes that the defects of Keller's method are those attendant on the use of chloroform and ether as a solvent. He finds that at a sufficiently low temperature brucine can be completely destroyed in the presence of strychnine by nitric acid, without loss of strychnine.—*Analyst, Lond.*, 1905, v. 30, pp. 261-264.

Lenton, Walter H., asserts that the U. S. P. assay for nux vomica is somewhat erratic and not comparable with the ferrocyanide method.—*Pharm. J., Lond.*, 1905, v. 21, p. 864.

Cowley thinks the simplicity of the U. S. P., VIII, method a decided advantage.—*Ibid.*, p. 889.

Francis, John M., believes that the difficulty of producing a powdered extract of nux vomica which upon dilution will yield a tincture of full strength, without precipitation, is as yet unsolved. While he admits that it may be too early to make a positive statement, his attempts to make a satisfactory extract of nux vomica by the U. S. P., VIII, formula have not been very encouraging. The process of extraction and purification he believes to be very tedious and expensive, and the resulting extract, after powdering, shows a marked tendency to revert to a solidified condition, due to the fact that milk sugar is not a good absorbent.—*Bull. Pharm., Detroit*, 1905, v. 19, p. 494.

An editorial, in commenting on the fluid extract of nux vomica of the U. S. P., VIII, says:

No directions are given for removing the fatty matter, and a satisfactory fluid extract can not be made by following strictly the pharmacopœial directions.—*Drug Topics*, 1905, v. 20, p. 213.

Kleinschmidt, A. A., characterizes the tincture of nux vomica as being one of the most objectionable preparations of the pharmacopœia, and believes that an assay for total alkaloids would have been better than for strychnine alone.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 404.

Thurston, Azor, examined five samples of tincture of nux vomica which ranged from 0.1383 to 0.2912 gm. alkaloids per 100 cc., being from 53.9 to 2.83 per cent below standard (U. S. P., VII).—*Proc. Ohio Pharm. Ass.*, 1905, p. 34.

Archetti, Andrea, presents a note on the preparation of tincture of nux vomica.—*Boll. Chim. Farm.*, 1905, v. 44, pp. 90-91.

Kinyon, H. E., believes that sluggish bowel movement, either from a nervous or muscular atony, may be cured by either *nux vomica*, strychnine, or arsenicum.—Hahnemann. Month., Phila., 1905, v. 40, p. 795.

OLEORESINA.

Francis, John M., points out that in the preparation of most official oleoresins acetone now replaces ether, and while it is admitted to combine the solvent properties of both alcohol and of ether, he believes that the resulting preparations may prove unsatisfactory because of the tendency to separate into a heavy portion corresponding to an alcoholic extract insoluble in ether and a lighter portion corresponding in a measure to the usual ether-extracted oleoresin, more or less insoluble in alcohol.—Bull. Pharm., Detroit, 1905, v. 19, p. 316.

OLEA.

FIXED OILS.

Schindler, J. (Ztschr. f. Unters. Nahr. u. Genussm., v. 9, p. 738), asserts that petroleum spirit (boiling between 30° and 45° C.) is preferred to ether for the determination of oil in seeds. He gives the yield of oil from 10 different seeds.—Pharm J., Lond., 1905, v. 21, p. 443.

Rakusin, M. (Apoth. Ztg., v. 20, p. 528), has determined the flash point of some vegetable oils. A table embodying his results is republished in the abstract.—Merk's Rep., N. Y., 1905, v. 7, p. 280.

Schroeder, August, reports some experimental work with several more or less rare oils and fats, including the oil from *Strychnos nux vomica*, *Hevea brasiliensis* Müller, and *Polygala senega* L.—Arch. d. Pharm., 1905, v. 243, p. 628.

An abstract (from La Revue de Chimie Industrielle) discusses the bleaching and concentration of vegetable oils.—Paint, Oil and Drug Rep., 1905, Aug. 21, p. 42.

Winckel, Max, discusses the decomposition of fats and the causation of rancidity. From his own experiments, and from a review of the literature, he concludes that the rancidity of fats is primarily due to the decomposition of the fatty acids under the influence of light and air.—Apoth. Ztg., Berlin, 1905, v. 20, p. 690.

Telle, Fernand (J. de Pharm. et de Chim., Paris, 1905, p. 180), considers the determination of the bromine number of fats as being more reliable than the corresponding determination of the iodine number. Unfortunately the great volatility of bromine and the corresponding variability of the solutions containing it are difficult to overcome.—Pharm. Zentralh., 1905, v. 46, p. 686.

An abstract figures and describes an apparatus that is designed to facilitate the determination of the iodine number of fats and fatty oils.—*Pharm. Ztg.*, 1905, v. 50, p. 1097.

An unsigned article discusses the valuation of lubricating oils, includes a description of the properties of a good lubricating oil and the determination of the free fatty and mineral acids.—*Chem. Eng.*, 1905, v. 3, pp. 10-19 and 87-94.

Filippo, Suzzi, discusses the use of mineral oils in the determination of the boiling point of oils.—*Boll. Chim. Farm.*, Milano, 1905, v. 44, pp. 301-308.

Just's *Botanischer Jahresbericht* (for 1905, v. 33, p. 779 and pp. 784-786) contains a number of references on vegetable oils, fats, and waxes, their origin and their use.

VOLATILE OILS.

An editorial expresses the belief that it is premature for methods of assay to be placed in the pharmacopœia which can be properly carried out only by skilled analysts and which are of so recent a date that few pharmacists in the retail business have ever heard of them, least of all tried them practically.—*Drug Topics*, N. Y., 1905, v. 20, p. 215.

Umney and Bennett assert that—

Viewed all around, there can be no question that the monographs are in themselves models of what such monographs intended for guidance in medicine should be, and in our opinion they go very decidedly further and are likely to be of value to all manufacturing pharmacists, also to those handling essential oils, and record the principal features in a concise form for judging.—*Pharm. J.*, Lond., 1905, v. 21, p. 143.

In the Spanish Pharmacopœia the essential oils are described as "Essentia," the synonym being "Oleum volatile." There are 19 volatile oils official: Bitter almonds, anise, orange flowers, bergamot, cinnamon, cajaput, citron, cloves, lavender, eucalyptus, lemon, peppermint, mustard, orange, rosemary, sandalwood, sassafras, thyme, and turpentine.—*Farmacopea Oficial Española*, 1905.

Umney and Bennett publish a comprehensive report on Sicilian essential oils, including peppermint and origanum. origanum oils of commerce, thyme oils, geranium, pennyroyal, lemon leaves, and nepeta.—*Pharm. J.*, Lond., 1905, v. 21, p. 860.

Sadtler, S. S., presents a study of the sulphite method for determining some aldehydes and ketones in essential oils. Among the products that are discussed are citral, cinnamic aldehyde, carvone, pulegone, benzaldehyde, and vanillin.—*J. Am. Chem. Soc.*, 1905, v. 27, pp. 1321-1327.

Schimmel & Co. point out that the method devised by S. B. Schryer (*Analyst*, 1900, v. 25, p. 18) for the determination of phenols in

essential oils is only applicable to oils which are simple mixtures of phenols and terpenes.—Analyst, London, 1905, v. 30, p. 62.

Wallach and Köhler discuss the constitution of eucarvone and its reduction products, and point out that von Baeyer's formula for eucarvone is not in accord with several properties of the compound.—Abstr. in J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 455 (from Annalen, 1905, v. 339, pp. 94-116).

A communication from U. S. Consul-General Skinner, Marseille, France, gives some account of the methods that are in use in Southern France for the production of essential oils and pomades. The article refers specifically to the production of the so-called oil of geranium.—Western Druggist, Chicago, 1905, v. 27, pp. 80-81.

Just's Botanischer Jahresbericht (for 1905, v. 33, part 3, pp. 787-788) contains a number of references that are of interest in connection with the general subject of essential oils.

Metzel, Richard, presents a contribution to the study of the pharmacologic properties of terpenes and terpene derivatives.—Arch. internat. de Pharmacod. et de Thérap., 1905, v. 14, pp. 351-354.

OLEUM AMYGDALÆ AMARÆ.

Umney and Bennett point out that the specific gravity of oil of bitter almond has been lowered from 1.060 to 1.070 at 15° C. to 1.045 to 1.060 at 25° C., which is a reduction more than proportionate to the different temperatures at which the determination is now made. In discussing the benzaldehyde determination they point out that the small quantity of oil required to be used is rather disadvantageous, and their results rather lead them to believe that the ordinary aldehyde absorption process, as used for the determination of cinnamic aldehyde in cassia oil, is preferable.—Pharm. J., Lond., 1905, v. 21, p. 145.

Lückner, Ed., reports autoxydation in a sample of oil of bitter almond that had been carefully preserved and securely corked.—Apoth. Ztg., Berlin, 1905, v. 20, p. 1044.

An abstract (from Pharm. Ztg., 1905, v. 50, p. 177) discusses the preparation of bitter almond water of the Ph. Germ., IV, and points out that maceration of the press cake should not be prolonged beyond six hours as the yield of HCN is lessened; the distillation requires one and one-half to two hours.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 521.

An abstract (from Brit. Med. J., Lond.) reports a case of poisoning by bitter almond oil.—Drug Circ. & Chem. Gaz., 1905, v. 49, p. 229.

OLEUM AMYGDALÆ EXPRESSUM.

Wetterstroem, Theo. D., asserts that oil of peach kernel is extensively sold as oil of sweet almond.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 312.

Schimmel & Co. report that the harvest of damascene apricot kernels is a small one. In good years the crop amounts to 8,000 bales; in 1904 it was 5,500 bales, and in 1905 it will be only 2,000 to 2,500 bales.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., p. 10.

OLEUM ANISI.

Schimmel & Co. discuss the production and the prices of oil of anise with some figures on the annual production of anise in Russia. They also report that a sample offered as anethol was found to be an inferior preparation, and did not possess the anethol content of a good oil of anise.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., pp. 11–12.

Schimmel & Co. also discuss the production of oil of star anise and quote some figures indicating the imports of this oil into Hamburg for the years 1903 and 1904.—*Ibid.*, pp. 65–66.

Umney and Bennett point out that—

The optical rotation should read *laevo gyrate up to* -2° , which is in accordance with our observations based upon the examination of a very large number of samples.—Pharm. J. Lond., 1905, v. 21, p. 144.

Riedel's Berichte points out that the higher limitation of the Ph. Germ., IV, on the boiling point of oil of anise, is rather low. The variations observed ranged from 232.1° at 725 mm. to 236.3° at 785 mm. pressure.—Riedel's Berichte, Berlin, 1905, p. 48.

OLEUM AURANTII CORTICIS.

Schimmel & Co. discuss some of the economic problems that are involved in the production and marketing of oil of bitter almonds.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.–May, p. 36.

Umney and Bennett point out that the optical rotation of not less than $+95^{\circ}$ is perhaps a little higher than necessary; over $+92^{\circ}$ would probably have been a sufficiently stringent test.—Pharm. J., Lond., 1905, v. 21, p. 145.

OLEUM BETULÆ.

Umney and Bennett point out that while this oil is stated to have the same properties as methyl salicylate, no references are made under oil of gaultheria to its similarity to Ol. Betulæ.—Pharm. J., Lond., 1905, v. 21, p. 145.

von Soden and Elze have examined the ethereal oil of birch buds, and find that it contains (1) a paraffin; (2) an ester not yet investigated; (3) a primary sesquiterpene alcohol, betulol, which is described.—J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 451 (from Ber., 1905, v. 38, pp. 1636–1638).

OLEUM CAJUPUTI.

Umney and Bennett believe that a minimum of 50 per cent of cineol would be more in accordance with the minimum specific gravity requirement; they also point out that there is one test, the test for the absence of copper, which is not quite clear, and assert that—

Should such a test be insisted on, there would be no necessity for the inclusion in the description of the words "a greenish liquid," as the green color of cajuput oil is entirely removed by the shaking with a solution of ferrocyanide of potassium, indicating that it is due to the presence of copper.—Pharm. J., Lond., 1905, v. 21, p. 145.

See also Semi-Ann. Rep., Schimmel & Co., 1905, Apr.–May, p. 12.

Geerligs. H. C. Prinsen (from Pharm. Weekbl.) points out that the green color of cajuput oil is due to the presence of copper, this being dissolved by the butyric and valeric acids and the esters of these acids which are contained in the oil; this he demonstrates by experiments with the purified oil from which the acids and esters had been completely removed.—J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 223.

Schimmel & Co. give the quantity of this oil imported into the United States as having increased from 1783 pounds in 1902 to 31,137 pounds in 1904.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., p. 14.

OLEUM CARI.

Schimmel & Co. discuss the production of caraway seed, the marketing of a chemically pure carvone, the constants of the latter, and the isolation of several hitherto unknown bodies from oil of caraway. These latter are given as (1) a small quantity of a base with narcotic odor, which was not examined further; (2) dihydrocarvone, the constants and properties of which are enumerated; (3) dihydrocarveol, the behavior, constants, and properties of which are also enumerated.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.–May, pp. 19–21.

Schimmel & Co. report finding adulterations of carvone (carvol). One sample, in addition to being adulterated with 15 per cent of alcohol, was so exceptionally deficient in solubility as to clearly evidence the inferior quality of the base used.—*Ibid.*, Oct.–Nov., p. 14.

Umney and Bennett point out that no process has been included for the determination of carvone, but that the physical characters enumerated should suffice to ensure an oil containing over 50 per cent carvone.—Pharm. J., Lond., 1905, v. 21, p. 145.

Riedel's Berichte reports that the limitations of the boiling point of oil of caraway, 229 to 230° C., as given in the Ph. Germ., IV, were found to be limited to a barometric pressure of from 755 to 770 mm.—Riedel's Berichte, Berlin, 1905, p. 48.

OLEUM CARYOPHYLLI.

Umney and Bennett assert that—

It has been shown that the strength of alkaline hydroxide solution used for absorption of the phenols makes some little difference in the percentage recorded (see Year Book of Pharmacy, 1903, p. 64), and our experience shows that the difference in absorption of phenols, using 5 and 10 per cent solutions of caustic potash, is 84 per cent in the former case and 89 in the latter, where the combined eugenol is entirely decomposed."—Pharm. J., Lond., 1905, v. 21, p. 145.

Riedel thinks the requirement in the Ph. Germ., IV (also in the U. S. P., VIII), that eugenol should have a boiling point varying from 250° to 253° is too low. The figures given by Hoffman, 250° to 260°, are thought to be more nearly correct.—Riedel's Berichte, Berlin, 1905, p. 49.

Schimmel & Co. think it advisable to judge of the value of clove oil according to its eugenol content, particularly as the refractive index alone can not be taken as a standard of the eugenol content.—Schimmel & Co., 1905, Apr.–May, p. 24.

Vanderkleed, Charles E., reports that three samples of oil of cloves all assayed above 73 per cent of eugenol.—Proc. Pennsylvania Pharm. Ass., 1905, p. 54.

The British vice-consul in Pemba reports that the yield of the clove harvest in 1904 reached the exceptional height of 14,447,600 pounds against 5,552,700 pounds in 1903, and 7,462,300 pounds in 1902.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., p. 20.

Frankforter and Lando discuss eugenol and certain of its derivatives.—J. Am. Chem. Soc., 1905, v. 27, p. 641.

Schimmel & Co. describe "Caryophyllin" as being a crystallizable substance which is present in the closed flower buds of the clove, *Caryophyllus aromaticus* L. It is said to have the composition $C_{10}H_{16}O$. Meyer and Hönigschmid (Monatsch. f. Chemie, v. 26, p. 379) record a detailed examination of this substance, and conclude that the proper molecular formula would be four times the formula disclosed by the analysis.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., pp. 20–22.

OLEUM CHENOPODII.

Eberle, E. G., mentions *Chenopodium anthelminticum* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 304.

The Bureau of Plant Industry reports the successful cultivation of American wormseed (*Chenopodium anthelminticum*); the experimental plat yielding at the rate of somewhat over 1,000 pounds per acre.—Ann. Rep. U. S. Dept. Agric., 1905, p. 148.

OLEUM CINNAMOMI.

Lloyd, John Uri, asserts that—

Oil of cinnamon differs in quality, as concerns both its origin and its manipulative course, as it wanders from its Oriental home to the hands of the consumer. Need it be said that the label, without a responsible firm behind it, is not a guarantee of the contents of the bottle.—Pharm. Rev., 1905, v. 23, p. 300.

Vanderkleed, Charles E., says that two out of three samples examined indicated the presence of rosin, and assayed 67 and 75 per cent of cinnamic aldehyde, respectively.—Proc. Pennsylvania Pharm. Ass., 1905, p. 54.

A communication to the committee on adulteration of the N. W. D. A., referring to oil of cassia, says:

We have frequently received this in original packages and found it had been opened and plugged at the bottom. In regard to this we find it a very hard matter to get the pure article.—Paint, Oil and Drug Rep., 1905, Oct. 6, p. 15.

Schimmel & Co., point out that the adulteration of oil of cinnamon with colophony and similar resins appears once more to be gaining ground in China, without the purchasers being able to prove a deficiency in the aldehyde content of the oil. Practically all of the parcels examined did not at all, or at least only partially, pass the lead acetate test of the Ph. Germ., IV.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.-May, p. 21.

Schimmel & Co. discuss the fluctuations in the price of cassia oil from 1886 to date. They say:

A strict control of the aldehyde content of this oil is strongly recommended, as our observations have led to the result that in many cases the simple statement of the content can not be relied upon.—*Ibid.*, Oct.-Nov., p. 16-17.

Umney and Bennett point out that the U. S. P., VIII, oil of cinnamon must not be confused with the oil of cinnamon of the Ph. Brit., as the latter is derived from *C. zeylanicum*. The title is rather misleading, especially as the two barks (*C. saigoncum* and *C. zeylanicum*) are official, while the bark of *Cinnamomum cassia* is not. As a flavor, they believe that the oil from *Cinnamomum zeylanicum* is to be preferred despite the fact that it contains less of the medicinally valuable cinnamic aldehyde. The limit of not less than 75 per cent of aldehydes, by volume, they believe to be a fair one, as good oils should contain from 80 to 85 per cent, by volume, of aldehydes.—Pharm. J., Lond., 1905, v. 21, p. 145.

Brandel, I. W., discusses the composition of the adulterations that have been recorded in current literature; he also records a modification, by Panchaud, of the bisulphite method for the assay of cinnamic aldehyde and points out that another method of assay, by Harms, depends on the production of cinnamic aldehyde semioxamamazine.—Pharm. Rev., 1905, v. 23, p. 382.

OLEUM COPAIBÆ.

Umney and Bennett point out that while there is a requirement that oil of copaiba should be laevo-gyrate, no limits are given.—Pharm. J., Lond., 1905, v. 21, p. 146.

Schimmel & Co. abstract a paper on gurjun balsam describing the method of collecting and the annual yield. The properties and uses of gurjun balsam are also enumerated.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.-May, pp. 48-49.

Schimmel & Co. enumerate the constants found in a gurjun balsam, which had been imported directly from the East Indies.—*Ibid.*, Oct.-Nov., p. 39.

OLEUM CORIANDRI.

Schimmel & Co. suggest that the scarcity of oil of coriander is due to the increased consumption in connection with the chocolate industry.—Semi-Ann. Rep., 1905, Apr.-May, p. 26.

OLEUM ERIGERONTIS.

Eberle, E. G., mentions *Erigeron canadense* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., v. 53, 1905, p. 305.

Rabak, Frank, reports on a study of oils distilled from fresh and from freshly dried herb of *Erigeron canadense*. A comparison of the constants of the oils thus obtained shows a decided difference in the ester and in the saponification numbers and a less marked difference in the acetylation number.—Pharm. Rev., 1905, v. 23, p. 81. See also Semi-Ann. Rep., Schimmel & Co., 1905, Oct.-Nov., pp. 23-24.

OLEUM EUCALYPTI.

Umney and Bennett point out that no particular source for the derivation of oil of eucalyptus is given in the U. S. P., VIII, and express the opinion that 55 per cent of cineol would be a better minimum for an oil for medicinal purposes.—Pharm. J., Lond., 1905, v. 21, p. 146.

Vanderkleed, Charles E., examined 4 samples, the best assaying 63.56 per cent cineol (eucalyptol); the poorest, 36.3 per cent. The latter and one other sample consisting largely of oil of *Eucalyptus amygdalina*, not *Eucalyptus globulus*.—Proc. Penna. Pharm. Ass., 1905, p. 54.

Gane, E. H., reports a sample of oil of eucalyptus which contained castor oil.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.

Bennett, C. T., calls attention to extensive adulteration of oil of eucalyptus with castor oil, to the amount of from 12 to 20 per cent. He points out that these adulterated oils comply with the several tests of the Ph. Brit., IV, and enumerates their characteristics. In

conclusion he points out that an admixture of from 5 to 10 per cent of castor oil, in eucalyptus oil of good quality, may easily be overlooked unless special tests are applied.—Chem. & Drug., 1905, v. 66, pp. 33–34.

Umney and Bennett report a study of the essential oil of *Eucalyptus polybractea* which, judged by the cineol content (79 to 80 per cent) appears to be of the highest medicinal value—not even second to the oil of *Eucalyptus globulus*.—Year Book of Pharmacy, 1905, p. 80 (from Pharm. J., Lond., v. 20, p. 143).

An abstract (from Bull. of the Imp. Inst., 1905, v. 3, pp. 4–6) enumerates a number of eucalyptus oils from New South Wales which were found to contain the “peppermint ketone.”—J. Soc. Chem. Ind., Lond., v. 24, p. 749.

Baker and Smith discuss some West Australian eucalypts and their essential oils. They include brief botanical descriptions and some account of the results of chemical analyses of *E. calophylla*, *E. diversicolor*, *E. salmonophloia*, *E. redunca*, *E. occidentalis*, *E. salubris*, *E. marginata*, and *E. gomphocephala*.—Pharm. J., Lond., 1905, v. 21, pp. 356, 382.

Schimmel & Co. assert that at the present time Australia controls the market in the oils rich in eucalyptol, no other source of supply being able to compete against such enormous production. They also direct attention to the work that is being done by J. H. Maiden in connection with his compilation, “A critical revision of the genus *Eucalyptus*,” and outline the contents of the sixth number of this comprehensive work.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., p. 33.

Taylor, H. S. (Lancet, Lond., 1905, II, p. 963), reports a case of acute poisoning by eucalyptus oil.—Reference from Ind. Med., 1905, p. 1137.

OLEUM FENICULI.

Schimmel & Co. discuss some of the economic questions bearing on the production and the price of oil of fennel.—Semi-Ann. Rep., 1905, Apr.–May, p. 39.

Umney and Bennett point out that there is usually some difficulty in starting crystallization unless a crystal of anethol is available. They also assert that they have not met with any oil of fennel sophisticated with volatile oils containing phenols, for which a test is included in the U. S. P., VIII.—Pharm. J., Lond., 1905, v. 21, p. 146.

Semmler, F. W., discusses the structural formula for fenchone and some of the possible derivatives.—Chem. Ztg. Cöthen, 1905, v. 29, p. 1313.

OLEUM GAULTHERIÆ.

Umney and Bennett point out that reference to the occasional reddish tint of oil of wintergreen is omitted. In several samples re-

cently examined by them this reddish tint was most pronounced.—Pharm, J., Lond., 1905, v. 21, p. 146.

Ziegelmann, E. F., reports some experiments with freshly distilled oils of wintergreen and birch from authentic sources. He enumerates the constants obtained and describes the methods followed.—Pharm. Rev., 1905, v. 23, p. 83.

OLEUM GOSSYPII SEMINIS.

Schwartz, D., in a paper read before the Am. Ass. Adv. Sc., 1905, discusses the refining, pressing, grading, and uses of cotton seed oil. He estimates that 75 per cent of the annual production of 120,000,000 gallons of oil is used for food purposes.—Exp. Sta. Rec., 1906, v. 17, p. 613.

An abstract, discussing the tests for cotton seed oil, asserts that the Becchi reaction, substantially that adopted by the Ph. Brit., is well known to be unreliable.

Raikow (Chem. Ztg., 1905, pp. 562-583) claims to oxidise cotton seed oil with potassium permanganate and cause it to lose the property of yielding the Halphen reaction. He therefore considers the color due to an unsaturated acid, and his conclusion is probably correct, Halphen to the contrary notwithstanding.—Chem. & Drug., Lond., 1905, v. 67, p. 67.

Halphen, G., discusses the experiments made by Raikow, and expresses the belief that the hypothesis proposed by the latter is not justified.—Ann. de chim. analyt., Paris, 1905, v. 10, p. 11.

Tolman, L. M., quotes a cold test for cotton seed oil, presented by the New York Produce Exchange, as follows:

A regular 4-ounce sample bottle filled with the oil to be tested, with a thermometer inserted through the cork, is hermetically sealed. The oil is then heated slowly to a temperature of 80° F. and held at that temperature for not exceeding fifteen minutes, it should remain clear, brilliant, and limpid for at least five hours at 32° F.—Proc. Ass. Off. Agr. Chem., 22 Ann. Conv., p. 67.

Emmett and Grindley review the literature on the presence of cotton seed oils in lards, from hogs fed upon cotton seed meal, and recount a series of experiments made to determine the presence of cotton seed oil. They conclude that these lards do contain a vegetable oil, and that they appear at least to contain three distinct constituents of cotton seed oil. It would therefore appear that a part at least of the oil existing in cotton seed meal is absorbed in the case of hogs fed upon this ration by the animal and transmitted in its unaltered condition to the fat cells.—J. Am. Chem. Soc., 1905, v. 27, pp. 263-270.

Tolman, L. M., reports a series of experiments to determine the presence or absence of phytosterol in lard from cotton seed meal fed hogs. He concludes that this lard does not contain phytosterol, that added cotton seed oil can be detected by the phytosterol acetate

method of Böhmer, and that heated cotton seed oil, which does not give the Halphen test, can be detected by this method. He also criticises the paper referred to above.—*Ibid.*, pp. 589–596.

OLEUM HEDEOMÆ.

Umney and Bennett point out that their experience with American oil of pennyroyal is comparatively limited, but that examination of European samples of Spanish, French, and Portuguese origin show that these, as a rule, have a specific gravity within the limits of 0.935 to 0.945 at 15° C.—*Pharm. J.*, Lond., 1905, v. 21, p. 146.

OLEUM JUNIPERI.

Umney and Bennett point out that the solubility test of oil of juniper is a little too stringent, as it will exclude some pure oils except freshly distilled.—*Pharm. J.*, Lond., 1905, v. 21, p. 146.

Ströcker (from *Pharm. Post*) has examined samples of Hungarian oil of juniper, which is obtained as a by-product in the manufacture of gin, and finds that the better quality corresponds fairly well to the requirements of the *Ph. Austr.* He gives the constants found, and concludes that for the preservation of the oil it is important that air be excluded.—*Pharm. Zentralh.*, 1905, v. 46, p. 823.

Brandel, I. W., refers to two oils originating from Russia which showed dextro-rotation of +7° to +8°. This deviation in the optical behavior appears to be due solely to the origin of the oils, for in other respects the oils did not differ from a normal distillate.—*Pharm. Rev.*, 1905, v. 23, p. 340.

Delphin, Af. T., discusses the testing of oil of juniper.—*Svensk. Farm. Tidskr.*, 1905, v. 9, pp. 81–83.

OLEUM LAVENDULÆ FLORUM.

Umney and Bennett point out that the U. S. P., VIII, includes no recognition of the determination of ester percentage, nor indeed any method for its valuation; in commenting further on the difficulties involved, they say:

One can see the difficulties of the compilers of the U. S. P. in trying to arrange a monograph that would exclude English oils, or, vice versa. Perhaps it was the wisest way out of the difficulty.—*Pharm. J.*, Lond., 1905, v. 21, p. 146.

Schimmel & Co. point out that among the more common adulterants detected during the last season in oil of lavender were oils of turpentine, rosemary, spike, and the so-called Spanish lavender oil, as to the botanical origin of which little or nothing definite is known. They enumerate the constants of these several oils and call attention to their differences.—*Semi-Ann. Rep.*, Schimmel & Co., 1905, Apr.–May, pp. 50, 54.

Schimmel & Co. illustrate and describe the manufacture of oil of lavender as conducted in the south of France. They discuss some of the adulterants used, and enumerate the constants found.—*Ibid.*, Oct.–Nov., pp. 40–42.

An unsigned article describes a lavender farm at Broadstone in Dorset, England.—*Brit. & Col. Drug.*, Lond., 1905, v. 48, p. 165.

OLEUM LIMONIS.

Umney and Bennett point out that the original figure for optical rotation of oil of lemon ($+60^\circ$) appeared to be a little high, and that a maximum of $+64^\circ$ might have been added. They also point out that—

While Sadtler's method for the determination of citral is perhaps the most satisfactory of published processes, it still leaves something to be desired. In the titration the end reaction is not sharp, and it is only likely to give good results in experienced hands. The quantity of sodium sulphite solution seems insufficient, as better results are obtained with double the quantity or the equivalent of a stronger solution. Our experiences with this process show from 3.8 to 4.4 per cent as normal limits for pure oil of lemon. Our experiences with this process show from 3.8 to 4.4 per cent as normal limits for pure oil of lemon.—*Pharm. J.*, Lond., 1905, v. 21, p. 146.

Schimmel & Co. discuss the properties of terpeneless oil of lemon and enumerate the constants found; they also present some observations on the aldehyde determination of oil of lemon.—*Semi-Ann. Rep.*, Schimmel & Co., 1905, Apr.–May, pp. 32–36.

Schimmel & Co. discuss the economic problems prevailing in connection with the production of oil of lemon. They also record the constants of an oil of lemon made in California.—*Ibid.*, Oct.–Nov., p. 27.

Berté, E., presents an indirect process for the determination of the aldehyde content of essential oil of lemon.—*Ibid.*, Apr.–May, p. 35, and Oct.–Nov., pp. 29–30; also abstr. in *Pharm. Ztg.*, Berlin, 1905, v. 50, p. 672.

Romeo, G., presents a monograph in which he describes a newly devised method for the quantitative estimation of citral, which is based on the fact that citral reacts with a solution of neutral and acid sodium sulphite, with formation of sodium citraltrihydrotrisulphonate, according to the equations given. The method appears to be similar to the determination of aldehydes and ketones as recommended by Sadtler.—*Sem-Ann. Rep.*, Schimmel & Co., 1905, Oct.–Nov., p. 30.

McGill, A. (from Lab. Inland Rev. Dept., Canad., Bul. 114, p. 15), reports a considerable range in alcohol strength and in lemon oil content of commercial extract of lemon. Of 110 samples examined,

2 contained 6 per cent or more of oil of lemon, and 78 less than 1 per cent. No methyl alcohol was found.—Exp. Sta. Rec., v. 17, No. 11, p. 1098.

The committee on adulteration report two samples of extract of lemon that contained methyl alcohol as the solvent. One sample was found to have been made from terpenes of oil of lemon.—Proc. Michigan Pharm. Ass., 1905, p. 78.

OLEUM LINI.

Wetterstroem, Theo. D., found linseed oil which contained from 2 to 100 per cent of mineral and resin oils.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 312.

LaWall, Charles H., examined 60 samples of linseed oil, of which 2 were adulterated.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.

OLEUM MENTHÆ PIPERITÆ.

Lyons, A. B., points out that in the assay process for menthol there is an inaccuracy in the calculation which would vitiate the result by fully 1 per cent. The calculation is so intricate that it is not easy to explain it clearly. It would be better merely to state arbitrarily that no more than a certain stated quantity of half-normal sulphuric acid V. S. should be required to neutralize the excess of alkali.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 260.

Umney and Bennett believe that the intention of the 8 per cent ester requirement is to obviate the inclusion of Japanese oil and to obtain an oil of as good value as possible. But they add:

It would appear to have gone very near precluding the use of some of the highest grade redistilled American peppermint oils. Certainly it will exclude some of the Mitcham and Cambridgeshire oils as normally distilled.—Pharm. J., Lond., 1905, v. 21, p. 147.

Mitchell, K. J., tested 12 samples and concludes that oil of peppermint is generally adulterated, chiefly through removal of part or all of the menthol.—Proc. Massachusetts Pharm. Ass., 1905, p. 105.

Gane, E. H., found a sample of oil of peppermint with a specific gravity of 0.903, rotation -16° , and not soluble in 10 volumes of 70 per cent alcohol. The sample contained cedar-wood oil and fixed oil to the extent of 10 per cent.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.

Henkel, Alice, discusses the several varieties of oil of peppermint, the source from which they are derived, the method of their production, the amount produced in 1904, the quantity produced in the United States, and the variation in price of the oil during the years 1873 to 1905, inclusive.—Bull. No. 90, Bur. Plant Ind., U. S. Dept. Agric., 1906, p. 28.

van der Wielen, P., describes a peppermint oil from Java. He asserts that the oil has a pleasant odor, different from that of ordinary peppermint, a faint bitter taste and a bright green color. He also enumerates the constants and properties, and points out that the oil contains a considerable quantity of pulegone, but little or no menthol and menthone.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 150 (from *Pharm. Weekbl.*, v. 41, p. 1081).

Schimmel & Co. discuss the supply of American, Japanese, English, and German oils of peppermint and quote a report by Umney and Bennett on the examination of Sicilian oil of peppermint.—*Semi-Ann. Rep., Schimmel & Co.*, 1905, Oct.-Nov., pp. 52-58.

Patch, Edgar L., reports examining 9 samples of spirit of peppermint: 3 had 10 per cent of oil; 1 had 1.5 per cent of oil and 70.5 per cent of alcohol; 1 sample had 0.5 per cent oil and only traces of alcohol, and 2 samples contained 4 per cent of oil of peppermint in wood alcohol.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

OLEUM MORRHUÆ.

Umney and Bennett outline a proposed description for the Ph. Brit. of refined cod liver oil.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 693 (from *Chem. & Drugg.*).

Parry, Ernest J., discusses some of the problems arising from the increase in the number of oils marketed as cod liver oil and gives some additional figures on cod liver oil standards.—*Ibid.*, p. 694 (from *Chem. & Drugg.*, v. 66, p. 491).

Brousfield, William (from *Chem. & Drugg.*), gives a description of the Lofoten Islands with some account of the manufacture of cod liver oil, a list of the fishing stations in Lofoten, and the cost of the oil.—*Western Druggist*, 1905, v. 27, pp. 435-438.

Kebler, Lyman F., announces that an investigation of both American and Norwegian cod liver oils is now being conducted by the Bureau of Chemistry, in collaboration with the Division of Foods of the Bureau of Fisheries, to determine their relative values chemically and medicinally. Thus far the results indicate that the American oil is the equal of the Norwegian.—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 491.

Thomson, H. C., describes a visit to Newfoundland, contributes some observations on the manufacture of cod liver oil, and describes the method of freezing out stearin.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 691 (from *Chem. & Drugg.*).

Lythgoe, Hermann C., discusses the optical properties of cod liver oil and of castor oil.—*Pharm. J., Lond.*, 1905, v. 21, p. 278 (from *J. Am. Chem. Soc.*).

Thomson and Dunlop point out that there is a close correspondence between the iodine number and the refractive index of fish liver oils

and the latter is, therefore, regarded as affording only corroborative evidence. The saponification is not of much value as a differential test, with the exception that dog fish oil has a very low value, corresponding with its high proportion of unsaponifiable matter, while porpoise blubber oil has a very high value, indicating the presence of volatile fatty acids. They assert that it is at the present time impossible to differentiate between cod, ling, coal fish, hake, whiting, haddock, and skate liver oils while the detection of small proportions of seal or whale oil or even of dog fish or shark liver oil is very difficult, though probably less than 5 per cent of porpoise oil could be detected.—*J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 741.*

Wetterstroem, Theo. D., is quoted as having examined 6 samples of Norwegian and 4 samples of Newfoundland cod liver oil, for both of which he gives the constants found. He also reports on 12 additional samples, one of which contained seal oil.—*Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.*

Kebler, Lyman F., is quoted as asserting that "Seldom does American cod liver oil of known purity comply with all U. S. P. requirements."—*Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.*

Burdo, D. L., examined 27 samples, the majority of which came up to the U. S. P. standard; 3 contained vegetable oils; 4 seal oil or other fish oils; 2 were strongly acid, and all but one were of standard specific gravity.—*Proc. Massachusetts Pharm. Ass., 1905, p. 105.*

Philip Röder reports that 5 samples of cod liver oil were examined and of these but one was even suspicious, because of its not giving a positive reaction with Kremel's test. As this sample was otherwise satisfactory its authenticity was not seriously questioned.—*Pharm. Post, Wien, 1905, v. 38, p. 390.*

Wiebelitz believes that the specific gravity for cod liver oil as defined in the Ph. Germ., IV, is too limited. He has met with good quality of oil that has a specific gravity of 0.9245, and believes that 0.932 is not too high.—*Pharm. Ztg., Berlin, 1905, v. 50, p. 779.*

An abstract from *Pharm. Post* gives the following figures as limits for good medicinal cod liver oil. Specific gravity, 0.920 to 0.931; acid value up to 3 in good oils and up to 10 in crude oils; saponification number, 17.0 to 19.5 per cent of potassium hydrate.—*Drug Topics, 1905, v. 20, p. 309.*

Moreau and Bietrix (*L'Union Pharm., 1905, p. 385*) assert that the frequently made statement that a cod liver oil which becomes cloudy at 0° C. or slightly below is adulterated is erroneous. They discuss the methods for obtaining and refining cod liver oils and point out that the behavior of these oils at low temperatures is entirely dependent on whether or not the oil is a natural oil or one that has been separated by having been exposed to low temperatures.—*Apoth. Ztg., Berlin, 1905, v. 20, p. 834.*

Barthe, L., believes that the determination of the congealing point of cod liver oil is a matter of considerable importance, particularly as Moreau and Bietrix have shown that absolutely pure cod liver oils will congeal at 0° C. As many of the commercial oils are treated at low temperatures to remove their low melting point fats, it may be well to require that pharmacopœias define whether or not such preliminary treatment is permissible.—Pharm. Ztg., Berlin, 1905, v. 50, p. 1010 (from Bull. des Sc. Pharmacol., Paris, 1905, pp. 204–206).

Mann, E. W., points out that a sample of cod liver oil may be largely adulterated and still give a satisfactory reaction with sulphuric acid.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 694 (from Chem. & Drugg.).

Schamelhout (Pharm. J., 1905) asserts that Kremel's nitric acid reaction is of doubtful value in the determination of the purity of cod liver oil, nor is it of much value in differentiating cod liver from other fish oils.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 694.

A correspondent (to Trade Review, St. Johns, N. F.) gives statistics of cod fish and cod liver oil produced in Norway during ten years:

	Fish.	Cod liver oil.		Fish.	Cod liver oil.
	<i>Millions.</i>	<i>Barrels.</i>		<i>Millions.</i>	<i>Barrels.</i>
1905.....	45	41,900	1900.....	39	33,100
1904.....	50	18,600	1899.....	38	35,500
1903.....	48	2,950	1898.....	42	26,600
1902.....	45	22,500	1897.....	62	35,600
1901.....	40	35,400	1896.....	52	24,000

Canad. Druggist, 1905, v. 17, p. 392.

OLEUM MYRISTICÆ.

Brandel, I. W., records from current literature some observations on the source and properties of oil of nutmeg.—Pharm. Rev., 1905, v. 23, p. 380.

OLEUM OLIVÆ.

Vanderkleed, Charles E., examined 13 samples of olive oil; 3 of these samples contained cotton seed oil and 2 were rejected on account of rancidity.—Proc. Pennsylvania Pharm. Ass., 1905, p. 54.

Kebler, Lyman F., reports a sample of olive oil, which was reported pure by different analysts, but which contained 17.5 per cent of peanut oil.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.

Halphen, G., outlines a method for the detection of olive oils obtained by extraction with carbon disulphide.—Ann. de Chim. Analyt., 1905, v. 10, pp. 333–334.

Milliau, M. E., proposes a modification of the test with nitrate of silver, which he believes will serve to distinguish cotton seed oil from other oils.—*Ibid.*, p. 9.

An abstract or translation (from Bull. de la Direction de l'Agricul. et du Com. de Tunis) discusses the properties of olive oils produced in the several districts of Tunis. The oils produced in the central districts congeal readily at low temperatures, and the demargarinization of these oils is discussed.—Paint, Oil and Drug Rep., 1905, Aug. 28, p. 38.

Richardson and Jaffe discuss the question of olive oils and free oleic acid in wool combing, and present tabulated results of analyses of various olive oils.—J. Soc. Chem. Ind., Lond., 1905, v. 24, pp. 534–536.

Just's Botanischer Jahresbericht (for 1905, v. 33, part 3, p. 783) contains several references to the geographical distribution of the olive tree, its cultivation, and the manufacture of olive oil.

OLEUM PICIS LIQUIDÆ.

Brandel, I. W., gives some account of the production, properties, and composition of American pine tar oil and the pine tar oil from Finland.—Pharm. Rev., 1905, v. 23, p. 326.

OLEUM PIMENTÆ.

Umney and Bennett point out that the lowering of the range of specific gravity is certainly an advantage, for the typical aromatic bodies characteristic of oil of pimenta are those with the lower specific gravity, although, perhaps, they do not add to its medicinal value. All of the tests, as in the case of oil of cloves, for other phenol bodies have been omitted.—Pharm. J., Lond., 1905, v. 21, p. 147.

OLEUM RICINI.

Eberle, E. G., mentions *Ricinus communis* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Osborne, Mendel, and Harris review the literature relating to the examination of the proteins of the castor bean, and record experiments conducted to determine the nature of these protein constituents.—Am. J. Physiol., 1905, v. 14, pp. 258–286.

Finnemore and Deane review the literature on ricinine, ricin, ricinoleic acid, and other fatty acids. They conclude that their results show that the purgative action of castor oil is due to the fatty acids, but it is not quite clear whether ricinoleic acid has been obtained absolutely pure, or that it is the only purging fatty acid in the oil; in any case it appears that there must be other undiscovered acids.—Pharm. J., Lond., 1905, v. 21, p. 137.

Lythgoe, Hermann C., discusses the optical properties of castor oil and cod liver oil.—*Ibid.*, p. 277 (from J. Am. Chem. Soc.).

Zimmermann, A., discusses the varieties of "*Ricinus*," the uses and methods of preparing the oil, the cultivation of the plant, enumerates the regions where it has been cultivated, and quotes some of the literature relating to the plant and its uses.—*Der Pflanze*, Tanga, 1905, v. 1, pp. 76-88.

Wright, H. (Rep. of Expt. Stat. Paradeniya, Ceylon), reports some experiments in the cultivation of *Ricinus communis* in Ceylon.—*Circ. & Agric. J. R. Bot. Gard., Ceylon*, 1905, v. 3, pp. 160-163.

Just's *Botanischer Jahresbericht* (for 1905, v. 33, part 3, pp. 777-778), contains several additional references bearing on the cultivation of the castor oil plant and the diseases affecting it.

OLEUM ROSÆ.

Umney and Bennett point out that the U. S. P., VIII, is the first pharmacopœia to include the saponification value for oil of rose. They also assert that—

Given that the physical and chemical characteristics indicate purity, then it is advantageous not to have a higher congealing point than 20° C., as a higher boiling point indicates naturally a greater proportion of odorless stearopten.—*Pharm. J., Lond.*, 1905, v. 21, p. 147.

An abstract quotes the limits of composition and the constants of Bulgarian oil of rose as given in Schimmel & Co.'s report for 1904, Oct.-Nov., p. 81.—*Analyst, Lond.*, 1905, v. 30, p. 65.

Schimmel & Co. present some observations on the economic questions involved in the production of rose oil, the destination of the Turkish oil of rose, and the amounts exported during the years 1898 to 1904, inclusive.—*Schimmel & Co., Semi-Ann. Rep.*, 1905, Apr.-May, pp. 67-69.

Koch, Felix J., presents a description of the home of oil of rose, the country, people, soil, method of planting and gathering roses; also some account of the distilling plants and the methods of marketing oil of rose.—*Western Druggist*, 1905, v. 27, p. 562.

OLEUM ROSMARINI.

Umney and Bennett are disposed to think the minimum percentage of borneol, 15 per cent, somewhat high, and suggest that 12.5 per cent would have been quite high enough. [U. S. P., VIII, 1907, reduced to 10 per cent.]—*Pharm. J., Lond.*, 1905, v. 21, p. 147.

Schimmel & Co. discuss the adulteration of rosemary oil with camphor oil fractions and enumerate the constants of the latter.—*Schimmel & Co., Semi-Ann. Rep.*, 1905, Apr.-May, pp. 69-70.

Schimmel & Co. illustrate the production of oil of rosemary on the island of Lesina and enumerate the constants found in an oil from Tunis, in the production of which probably other plants than *Rosmarinus officinalis* L. have been used.—*Ibid.*, Oct.-Nov., p. 61.

OLEUM SABINÆ.

Umney and Bennett point out that the requirement that the oil be distilled from the fresh tops is a very important feature, as it practically eliminates a considerable proportion of the woody plants from which the oil has been distilled in the south of France, which resulted in an oil widely different from that official, either in the present or the previous edition of the U. S. P. They add:

We are disposed to think, from the examination we have made of savin distillates, that there is a considerable difference in the product obtained in different countries, and there is, possibly, a slight difference in the variety of the savin itself.—*Pharm. J.*, Lond., 1905, v. 21, p. 148.

Ziegelmann, F. E., discusses the requirements for oil of savin in the several pharmacopœias and enumerates the constants determined from a sample of oil distilled from the dry drug.—*Pharm. Rev.*, 1905, v. 23, p. 22.

OLEUM SANTALI.

Umney and Bennett point out that—

The inclusion of a test for absence of chloroform is interesting as showing how what one may call a local sophistication may result in the inclusion of a special test for the detection of that particular adulterant.—*Pharm. J.*, Lond., 1905, v. 21, p. 148.

Vanderkleed, Charles E., reports that of dozens of samples examined, only five assayed less than 90 per cent of santalol, and in no case was any adulterant found, except that in possibly two cases some West Indian oil was present.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 55.

Vanderkleed, Charles E., calls attention to two errors in the method for the determination of santalol, as given in the English translation of Gildemeister and Hoffman's "Volatile oils," to an improvement proposed by Wielen in the *Chemiker Zeitung*, and to an error in Schimmel & Co. Semi-Annual Report for April, 1898.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 193; also *Pharm. Era*, N. Y., 1905, v. 34, p. 77.

Siedler (*Apoth. Ztg.*, v. 19, p. 795) records the characteristics of santalol and of East Indian sandalwood oil.—*Analyst*, London, 1905, v. 30, p. 93.

Brandel, I. W., cites from the current literature several references to the properties and the adulteration of oil of santal.—*Pharm. Rev.*, 1905, v. 23, p. 378.

Wendt, Gustav, estimates the annual consumption of oil of santal to be upward of several hundred thousand kilos. This widespread use, and the accompanying comparatively high price, have led to widespread adulteration of this product.—Pharm. Ztg., Berlin, 1905, v. 50, p. 899.

Schimmel & Co. discuss the economic features connected with the production of sandalwood. The spread of the "spike" disease is referred to and exception is taken to the constants for oil of santal, proposed by Siedler (Apoth. Ztg., v. 19, p. 795), and particularly to the suggestion that santalol should be substituted in the pharmacopœia for oil of santal.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.–May, pp. 70–74.

Schimmel & Co., in discussing the production and shipments of sandalwood, conclude that the importance of the "spike" disease has been overestimated. They are inclined to think that their previous requirements for a rotatory power of -17° is rather high, and announce that in future they will not be able to adhere strictly to this.—*Ibid.*, Oct.–Nov., pp. 62–65.

Runge, P., reports that West Indian oil is frequently added to, or substituted for, the East Indian oil of santal. He points out that in addition to the specific gravity, rotatory power, solubility, santalol number and odor, Conrady's reaction is serviceable. This is applied by adding 7.5 cc. of a mixture of 9 parts of glacial acetic acid and 1 part of hydrochloric acid to 2 drops of the suspected oil. Pure East Indian oil produces a colorless solution, which retains this condition for at least ten minutes, whereas the usual adulterants yield within this time a rose to dark red coloration.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 522.

OLEUM SINAPIS VOLATILE.

Umney and Bennett assert that the method of assay adopted is decidedly better than that formerly official.—Pharm. J., Lond., 1905, v. 21, p. 148.

Riedel's Berichte points out that the boiling point of oil of mustard appears to be quite constant, varying from 149.3° at 715 mm. to 153.4° at 795 mm. pressure.—Riedel's Berichte, Berlin, 1905, p. 49.

OLEUM TEREBINTHINÆ.

Brandel, I. W., presents an exhaustive communication on oil of turpentine, in the course of which he reviews the literature relating to oil of turpentine, published during the past year, and gives some account of the origin, preparation, and properties of the oils of turpentine derived from several sources.—Pharm. Rev., 1905, v. 23, pp. 321–326.

Utz, F., reviews some of the later publications relating to oil of turpentine, compares some of the constants that have been reported, and, in conclusion, suggests the determination of the following: (1) Odor, color, and fluorescence, (2) specific gravity, (3) polarisation, (4) refraction, (5) testing with Herzfeld's apparatus, (6) refraction of portion insoluble in fuming nitric acid, (7) behavior with sulphurous acid, (8) Storch-Liebermann's reaction, (9) reaction with bromine and iodine, (10) determination of the iodine number, and (11) behavior with blood, fresh milk, etc., and with guaiac tincture or paraphenyldiamin.—*Pharm. Prax.*, 1905, v. 4, pp. 102-109.

Walker, Wiggins, and Smith assert that turpentine can be obtained from lightwood, by steam distillation, and that this turpentine is in every way the equal of the present commercial article, except the difference in odor. They include a detailed description of the apparatus and methods employed in its manufacture.—*Chem. Eng.* 1905, v. 3, pp. 73-84.

Thurston, Azor, points out that commercial oil of turpentine usually has a specific gravity of 0.8644 and a refractive index of 1.475. Four adulterated samples that he met with had a specific gravity of 0.8166, 0.8128, 0.8248, 0.7976, respectively, and it was almost impossible to get a reading on the refractometer.—*Proc. Ohio Pharm. Ass.*, 1905, p. 34.

Vaubel, Wilh., presents a comparative study of the constants for commercial oils of turpentine that are available in the literature.—*Ztschr. f. öffentl. Chem.*, 1905, v. 11, pp. 429-435.

Pancoast and Graham present tables of constants for samples of American, French, and Canadian oils of the coniferæ.—*Proc. Penna. Pharm. Ass.*, 1905, p. 184.

Herzfeld, H., points out that the oil obtained from the distillation of resinous wood has, within recent time, been refined to such a degree that now neither odor nor color reaction with caustic soda and concentrated hydrochloric acid can be used to distinguish it. This refined oil, however, when shaken with an equal volume of sulphurous acid solution is colored yellowish green, and can be detected when present to the extent of 10 per cent in oil of turpentine.—*Abstr. J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 108 (from *Ztschr. f. öffentl. Chem.*, v. 10, pp. 382-384).

Walker, Wiggins, and Smith discuss the steam distillation of light wood and outline a method for the production of an oil similar to the commercial oil of turpentine.—*Tech. Quarterly*, 1905, v. 18, pp. 301-312.

An abstract (from *Forestry and Irrig.*, v. 12, pp. 99-100) points out that the forest service has suggested further economy in the turpentine industry by demonstrating that at least an equal flow of resin

can be obtained from shallower and shorter faces. It is believed that with the diminution of the severity of the facing operation the ordinary term of three or four years during which a forest is now worked can be greatly increased.—Exp. Sta. Rec., v. 17, p. 979.

The committee on adulteration reports that three samples of oil of turpentine, obtained by the steam distillation of pine wood, were examined and found to differ from the ordinary oil of turpentine in that they did not give the hæmoglobin test.—Proc. Michigan Pharm. Ass., 1905, p. 80.

Schimmel & Co. record experiments made by different observers to devise tests for differentiating between turpentine oil and the several wood oils that are being marketed as substitutes for oil of turpentine.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.-Nov., pp. 67-71.

Utz, F., presents a didactic discussion of the limitations which should be made in the all too frequently misleading use of the name "oil of turpentine."—Pharm. Zentralh., 1905, v. 46, p. 681.

Schimmel & Co. agree with Utz (see reference above) that the designation "oil of turpentine" might well be reserved for the essential oil obtained by distillation with steam from the turpentine of various American and French species of *Pinus*, thus differentiating it from the oils obtained by means of superheated steam from wood rich in turpentine.—Semi-Ann. Rep., 1905, Oct.-Nov., p. 67.

Riedel's *Berichte* points out that the Ph. Germ., IV, gives the boiling point of rectified oil of turpentine as from 155° to 162° ; according to the experiments recorded by Riedel the boiling point at 760 mm. pressure may vary from 158.8° to 161.8° C.—Riedel's *Berichte*, 1905, p. 50.

OLEUM THEOBROMATIS.

Strube, F., reports finding an abnormal oil of theobroma from which a fraction was separated that did not congeal even after long standing in a cool place. The iodine number and the refractometer number were unusually high, the melting point was low, about 12° C., the genuine origin of the specimen was unquestioned and indicated a possible abnormality in the oil itself.—Ztschr. f. öffentl. Chem., 1905, v. 11, p. 215.

Rakusin (abstract from Chem. Ztg.) has made some investigations on the specific gravity of oil of theobroma, and finds that the figures given by Dietrich, and adopted in the U. S. P., are more correctly true than are the figures quoted by Hager, which Rakusin finds are too low.—Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 17.

Davis and McLellan suggest that, because of the difficulty of completely extracting the fat from cacao seeds, the previously made estimates of the fat content have been low. A number of extractions made by the authors showed an average oil content of 54.44 per cent,

or about 5 per cent higher than the figures given by Heisch and Zipperer.—Ztschr. f. Unters. Nar. u. Genussm., 1905, v. 9, p. 377.

An abstract from a monthly summary, Department of Commerce and Labor, contains an account of the history, description, cultivation, curing, and preparing of the several varieties of cacao.—Pharm. Era., N. Y., 1905, v. 34, p. 508.

An abstract (from Bull. des Sc. Pharmacol., Paris, 1905, p. 302) presents an enumeration of the countries producing and of the countries using cacao and the amount, in metric tons, that is produced and used. The annual consumption, 64,507 tons, in 1894, has been increased to 127,452 tons in 1903.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 386.

OLEUM THYMI.

Umney and Bennett suggest that oil of thyme might also find a place in a new Ph. Brit., and point out that the proportion of thymol and carvacrol (the two phenols) vary considerably in different samples of the oil, and especially in the samples of the closely allied organum oils imported from eastern Europe.—Pharm. J., Lond., 1905, v. 21, p. 148.

Schimmel & Co. discuss the priority of the suggestion of the use of soda lye for phenol determination in essential oils. Controverting the claims that are made by Umney, they assert that the method was first recommended by Gildemeister, in 1892, for the phenol determination in thyme oil.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.-May, p. 76.

Schimmel & Co. record some adulterations found in oil of thyme. One sample adulterated with oil of turpentine was particularly striking on account of its deficient solubility and low phenol content, 12.5 per cent; not soluble in 10 volumes of 80 per cent alcohol. Another sample was designated as "white" thyme oil, and had probably been mixed with a considerable quantity of camphor oil.—*Ibid.*, Oct.-Nov., p. 67.

OLEUM TIGLII.

Lloyd, John Uri, asserts that probably no one is in a position to say positively that he has ever used any croton oil pressed wholly from the seed of *Croton tiglii*, though he is not willing to assert that the oil in a state of absolute purity can not be obtained.—Pharm. Rev., 1905, v. 23, p. 300.

Mazzuchelli (Arch. Farmac. speriment., 1905, p. 223) says that, contrary to the assertion of various authors, petroleum benzin does dissolve castor oil, and that this fact can be utilized for the purpose of detecting croton oil when mixed with castor oil.—Am. Druggist, N. Y., 1905, v. 47, p. 202.

Kinyon, H. E., in discussing the treatment of constipation by medicines, points out that croton oil is valuable in lessened secretion of the intestinal juices or a too rapid absorption of the liquids of the colon.—Hahneman. Month., Phila., 1905, v. 40, p. 795.

OPIUM.

Bernström (Svensk. Farm. Tidskr., 1905) believes that the water content of opium is of comparatively greater importance than the extract content, and that pharmacopœial descriptions are usually lax in this regard. He found that the contained moisture, drying at 60° C., varied from 20.27 to 23.75 per cent, while at 100° C. it varied from 25.27 to 27.82 per cent. The ash of the water-free drug varied from 3.31 per cent for Persian to 7.89 per cent for manipulated Smyrna, which was found to be adulterated with lead filings.—Pharm. Ztg., 1905, v. 50, p. 960.

Williams, John K., from many experiments finds that the natural gum loses upwards of twenty per cent when sliced and air dried.—Proc. Connecticut Pharm. Ass., 1905, p. 51.

The revisors of Vienna pharmacies (Ztschr. d. österr. Apoth. Ver.) found opium that contained from 4.0 to 15.58 per cent of morphine; extract of opium varied from 2.0 to 37.1 per cent of morphine and tincture of opium 0.12 to 0.82 per cent of the same alkaloid. The microscope showed that the opium was contaminated with starch, flour, and powdered poppy capsules.—Pharm. Prax., 1905, v. 4, p. 38.

Wetterstroem, Theo. D., reports finding opium which contained from 5.78 to 33.9 per cent of water and from 7.46 to 13.34 per cent of morphine.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.

Vanderkleed, Charles E., reports 20 assays of powdered opium which varied from 11.38 to 15.5 per cent of morphine; 7 of the 20 samples were below the U. S. P. (1890) standard.—Proc. Pennsylvania Pharm. Ass., 1905, p. 57.

Moore, Russell W., asserts that the quality of opium coming into the port of New York is generally good. Of 309 samples examined only 19 were below the standard of 9 per cent of morphine.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 266.

Masson, V., describes a product that is being sold under the name "Smyrna" or "manipulated" opium and which consists of a mixture of the natural juice with substances more or less inert. The samples examined differed widely in composition and the components are frequently so altered that the active ingredients do not readily go into solution.—Analyst, Lond., 1905, v. 30, p. 310 (from J. de Pharm. et de Chim., 1905, v. 21, pp. 529-534).

Guiges, P., reports a study of three samples of opium marked, respectively: "Opium qualité supérieure," "opium qualité moyenne,"

and "opium qualité inférieure." These samples yielded from 3.60 to 6.15 per cent of ash and from 1.90 to 11.18 per cent of morphine.—*J. de Pharm. et de Chim.*, 1905, v. 22, p. 103.

Hood, C. S., in an article on Botany and its relation to the pharmacist discusses the cultivation of opium, the amount of this drug imported, and the possibility of its economic production in this country.—*Western Druggist*, 1905, v. 27, p. 774.

Weschke, Emil (from *Pacific Medical Journal*), reviews the available literature and recounts his own experience with the cultivation of opium and the opium poppy in southern Minnesota.—*Western Druggist*, 1905, v. 27, p. 512.

True, Rodney H., points out that many private experimenters have found that the Asiatic poppy does well over a large part of the country.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 273.

The Bureau of Plant Industry reports the successful cultivation of both the blue and white seeded varieties of poppy at Burlington, Vt. This material gave a favorable yield of crude morphine.—*Ann. Rep. U. S. Dept. Agric.*, 1905, p. 149.

Thoms, H., reports some experiments that were made in the cultivation of opium at Dahlen in connection with the work of the Pharmaceutical Institute.—*Arb. a. d. pharm. Inst. d. Univer. Berlin*, 1905, v. 2, pp. 144–155.

Harris, Wm., discusses the cultivation of opium and the differences between the products from Asia Minor, Egypt, Persia, and East India.—*Bull. Dept. Agric., Jamaica*, 1905, v. 3, pp. 78–84.

Peltriset, G. N. (from *Ann. de Pharm. de Louvain*), presents a comprehensive paper on opium, its production, and its uses. The paper as reprinted includes some reference to the cultivation of the poppy, collecting the crop, preparation of opium, medicinal opium, preparation of opium for smoking, ways in which opium is used, the opium smoker, and the opium eater.—*Nat. Druggist*, St. Louis, 1905, v. 35, pp. 40–41.

An abstract from the *Tropical Agriculturist* gives a description of the methods used in North India for the production of "raw" opium.—*Nat. Druggist*, St. Louis, 1905, v. 35, p. 302.

An editorial comments on the reports that have been made from time to time of efforts to produce opium in countries outside of Asia and the success that has attended these several efforts.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 100.

Braun, K., discusses the botany and the several varieties of poppy and the cultivation of this plant as it is carried on in various parts of Asia, Africa, Australia, America, and Europe. He also includes an extensive bibliography.—*Der Pflanze*, Tanga, 1905, v. 1, pp. 157–191.

Linde, O., discusses the possibility of producing opium, and argues that the production of a morphine-rich poppy plant is quite a possibility, and that the production of poppy seed would amply repay the cost of cultivation, apart from the opium produced.—*Just's Bot. Jahresber.*, 1905, v. 33, part 3, p. 226 (from *Apoth. Ztg.*, 1905, v. 20, p. 233).

Just's Botanischer Jahresbericht (for 1905, v. 33, part 3, p. 778) contains several additional references on the cultivation of the opium poppy and the production of opium.

Wood, S. C., gives an account of experiments made to develop a poppy plant that is rich in alkaloids.—*Pharm. Era*, 1905, v. 34, p. 507.

OPIMUM ASSAY.

Herting, Otto, believes that the correction in the method of assay for opium is a good one, and that the addition of limewater will serve to make the now official method preferable to that included in the *Ph. Germ.*, IV.—*Deut.-Amer. Apoth. Ztg.*, N. Y., 1905, v. 26, p. 71.

Bernström, G., reviews the several methods recommended for the assay of opium, and discusses the relative advantages, as also the relative value of hæmatoxylon and iodeosin as an indicator, pointing out that the latter is not free from objectionable features, particularly in the presence of narcotin.—*Svensk. Farm. Tidskr.*, 1905, v. 9, pp. 297-302 and 309-315.

Valenti, L. (*Giorn. di Farm. di Trieste*, 1905, p. 289), presents a comparative study of the different methods that have been proposed for the determination of morphine in opium, and recommends that of Flückiger (precipitation from a solution in ether alcohol). The only drawback is the solubility of the morphine in the solvent. This amounts to 0.118 gm. per 100 cc., which should be added to the weight of the morphine found.—*Analyst, Lond.*, 1905, v. 30, p. 337.

Petit, Arthur and Albert (*J. de Pharm. et de Chim.*, 1905, v. 21, pp. 107-111), outline the method of assay for opium adopted for the French Codex. The opium, after drying, is mixed with slaked lime, then mixed with water and allowed to stand for two hours, with occasional agitation. The mixture is transferred to a filter and an aliquot part of the filtrate is shaken with ether; ammonium chloride is then added, and the resulting mixture allowed to stand for twenty-four hours in a covered beaker. The resulting morphine is collected on a filter, washed, and weighed after being dried for two hours at 100° C.—*Analyst, Lond.*, 1905, v. 30, p. 207.

Mallinckrodt and Dunlap report some experiments on the assay of opium and the influence of meconic acid, particularly in the presence of lime salts.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 946.

Fromme, G., asserts that the separation of calcium meconate begins within six hours, and is sufficient to give abnormally high results when using the assay process of the Ph. Germ., IV. He reports the assay of four samples of opium, which serve to demonstrate the difference in apparent yield of alkaloid in six and in twenty-four hours.—*Geschäfts-Bericht von Caesar & Loretz*, in *Halle a. S.*, 1905, pp. 43–47.

Caesar and Loretz recommend the use of acetic ether in place of ether to promote crystallization of the morphine, and give details of a process based on this change.—*Geschäfts-Bericht von Caesar & Loretz*, in *Halle, a. S.*, 1905, p. 92.

Hauke, R. (*Pharm. Post.*) asserts that for the estimation of morphine in opium only the methods as outlined by Flückiger and E. Dietrich are to be considered. He believes that the former deserves to have the preference, though the method by E. Dietrich is characterized as being more accurate and, scientifically, more correct.—*Pharm. Prax.*, 1905, v. 4, p. 17.

Naylor, W. A. H., discussing the assay of opium, asserts that the process by Dowzard is to be preferred. Dott's process, he says, though excellent in many respects, requires 18 hours for the precipitation of the morphine. He also points out that if the morphine be washed until free from traces of ammonia it can be safely triturated in the manner suggested by Dowzard without previous drying.—*Pharm. J., Lond.*, 1905, v. 21, p. 125.

Kebler, Lyman F., comments on the literature relating to the assay of opium and gives in detail the following methods:

(1) The U. S. P., VIII, (2) U. S. P., VIII, modified by Lamar, (3) U. S. P., VIII, modified by Dohme, and (4) Stevens's with additions. A table embodying the results obtained by different analysts is appended.—*Proc. Ass. Off. Agr. Chem.*, 22 Ann. Conv., pp. 161–170.

Halle, Walter L., discusses the relations of thebaine to morphine and codeine, its structural formula and some of its derivatives.—*Chem. Ztg. Cöthen*, 1905, v. 29, p. 1266.

Knorr and Pschorr present a study of thebaine, including discussion of (1) Decomposition of morphothebaine, (2) thebainone, a ketone formed by the reduction of thebaine, (3) thebainone from codeinone, and (4) decomposition products from thebainone.—*Abstr. in Pharm. J., Lond.*, 1905, v. 21, p. 909.

Beuttner, E., discusses the difficulty of exhausting opium, particularly by percolation. He recommends, as the result of his experience, a combination maceration and percolation procedure. He does not believe that a percolation process, per se, is advantageously applicable to drugs that are soluble to the extent of 50 per cent of

their weight.—Schweiz. Wchnshr. f. Chem. u. Pharm., 1905, v. 43, p. 542.

Dohme, A. R. L., examined 5 samples of tincture of opium and found them to vary from 0.324 to 0.894 per cent of morphine in place of 1.35 per cent required by the U. S. P. (1890).—Proc. Maryland Pharm. Ass., 1905, p. 49.

Wetterstroem, Theo. D., reports that of 60 samples of tincture of opium examined, 2 contained wood alcohol, while of the remaining number, assayed by the U. S. P. (1890) method: 2 contained less than 0.3 per cent of morphine, 3 less than 0.60 per cent, 12 less than 0.9 per cent, 4 less than 1.0 per cent, and only 14 above 1.3 per cent. In this series the weakest contained 0.2 per cent and the strongest 1.568 per cent of morphine.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 187.

Thurston, Azor, reports examining 4 samples of tincture of opium which ranged from 42.8 to 16.03 per cent below the minimum U. S. P. (1890) requirement.—Proc. Ohio Pharm. Ass., 1905, p. 33.

An abstract from the annual report of Philip Röder, Wien, reports 6 samples which were found to vary from 0.750 to 1.070 per cent of morphine. Two samples of tinctura opii crocata were found to vary from 0.705 to 1.292 per cent of morphine.—Pharm. Post, Wien, 1905, v. 38, p. 393.

Caldwell, Paul, recommends making the deodorized tincture of opium directly from deodorized opium.—Drug. Circ. and Chem. Gaz., N. Y., 1905, p. 221.

Bird, F. C. J. (from Pharm. J., Lond.), outlines a method for the assay of camphorated tincture of opium.—Analyst, London, 1905, v. 30, p. 336.

Donnelly, M. F., examined 20 samples of camphorated tincture of opium. The specific gravity ranged from 0.931 to 0.998, while a standard U. S. P. sample gave 0.937. The extractive matter varied from 0.60 to 13.4 per cent, the U. S. P. standard sample being 6. The physical properties of the samples differed widely. The color varied from a very pale yellow to one as dark as laudanum. A number contained licorice.—Proc. Massachusetts Pharm. Ass., 1905, p. 102.

Kelly, E. F., reports progress on assay work done in connection with the powder of ipecac and opium.—Proc. Maryland Pharm. Ass., 1905, pp. 116–118.

An editorial outlines the proposed legislation in Victoria to regulate the sale of smoking opium. This legislation would provide for a license to sell opium under a complete system of registration of: (1) The name of the purchaser and his address. (2) the quantity purchased and the price. (3) the name of a legally qualified medical practitioner by whom the opium is prescribed.—The Australasian J. Pharm., 1905, v. 20, p. 266.

PANCREATINUM.

Hedin, S. G. (from *J. of Physiol.*, 1905, v. 32, p. 468), reports some experiments with tannin and trypsin to determine the activity of the latter.—*Biochem. Centralbl.*, 1905, v. 4, p. 268.

Ehrenreich, M. (*Arch. f. Verdauungs Krankh.*, Berlin, 1905, v. 40) discusses the unity and specific nature of pancreas trypsin.—Reference from *J. Am. M. Ass.*, 1905, v. 45, p. 1450.

Bergell and Schütze report that they were unable to produce an antiserum by injecting pancreatin solutions into rabbits or goats. While these preliminary experiments are not considered to be conclusive, the authors appear to think that it will be impracticable to form antibodies for such ferments as possess peptid-binding properties.—*Chem. Centralb.*, 1905, v. 76, p. 154.

PARALDEHYDUM.

Riedel's *Berichte* points out that the requirements of the Ph. Germ. IV, for a boiling point of from 123° to 125° was found to be practically correct for the ordinary variation in barometric pressure. The experiments recorded vary from 122.8° C. at 722 mm. pressure to 126.3° at 792 mm. pressure, indicating that the lower temperature given by the U. S. P., VIII, is rather too low.—Riedel's *Berichte*, Berlin, 1905, p. 50.

Kebler, Lyman F., reports finding a sample of paraldehyde containing 0.533 per cent of nonvolatile matter and congealing at 10° C. in place of near 0° as required by the U. S. P. VIII.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

PEPSINUM.

Schrumpf, P., outlines the preparation of pepsin by subjecting the mucous membrane of the pig's stomach to pressure, as in Buchner's work on yeast, and the liquid filtered through a Chamberlain filter. The pepsin separated from this filtrate by the cholesterol method was protein free. In some cases the solution had rennetic properties, in other cases not, a fact which tells against the view of Pawlow and Nencki that pepsin and rennin action are both due to the same molecule.—*J. Chem. Soc., Lond.*, 1905, v. 88, part 2, p. 556.

Bickel, Adolph (*Dtsch. Med. Wehnschr.*, 1905, p. 1383), demonstrates that pepsin is quite resistant to low temperatures and that even so low a temperature as liquified air does not materially impair its activity.—*Apoth. Ztg.*, 1905, v. 17, p. 727.

Lucas, E. W. (*Pharm. J., Lond.*, v. 19, p. 376), discusses the determination of the digestive power of pepsin and suggests a modification of the official process. He points out that coagulated egg white rubbed through a sieve is not sufficiently broken up and that

it is impracticable to weigh 0.005 gm. of such a hygroscopic substance.—*Year Book of Pharmacy*, Lond., 1905, pp. 275–276.

Löhlein, Walter, reports some additional experiments on the quantitative determination of pepsin by titration, proposed by Volhard in 1903 (*Münch. Med. Wchschr.*, 1903, No. 49). He reviews the several methods proposed for the determination of pepsin and records a series of experiments with Volhard's process which he outlines.—*Beitr. z. Chem. Phys. u. Path.*, 1905–6, v. 7, pp. 120–144.

O'Sullivan, James, outlines a method for determining the proteolytic activity of pepsin by determining the amount of nitrogen which goes into solution during proteolysis.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, pp. 830–832.

v. Fujitani, J., discusses the influence exerted by various neutral salts of inorganic bases. He records a number of experiments and concludes that boric acid, salicylic acid, sulphates, chlorates, nitrates, bromides, and iodides all serve to inhibit the action of pepsin. Many of the alkaloids, such as cocaine and quinine, also inhibit this action. A very few substances, among them caffeine and the acetates, appear to stimulate digestion.—*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 847 (from *Arch. internat. d. Pharmacodyn. et d. Thérap.*, 1905, v. 14, pp. 1–37).

Cobb, Percy W., presents a contribution to the knowledge of the action of pepsin with special reference to its quantitative estimation. He reports a series of experiments and concludes that results obtained by the albumin froth method of Bettman and Schroeder cannot justifiably be expressed in figures indicative of pepsin concentration, but only by such expressions as "strong," "very strong," "moderate," etc.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 479 (from *Am. J. Physiol.*, 1905, v. 14, pp. 448–464).

Blauvelt, Wm. H., records having used pepsin in connection with volatile oils and creosote as an excipient and recommends a trial in the proportion of about 1 grain of pepsin to one-half minim of volatile oil.—*Proc. N. Carolina Pharm. Ass.*, 1905, p. 37.

Caldwell, Paul, believes that the proneness of essence of pepsin to become cloudy and to precipitate is due to the presence of tannin in the wine. To obviate the difficulty he recommends the use of de-tannated wine.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 220.

Schirmer recommends the addition of 3 cc. of milk to each liter of wine of pepsin. The acid in the wine is thought to be sufficient to coagulate the casein of the milk and this serves as the clarifying agent.—*Pharm. Ztg.*, 1905, v. 50, p. 1008.

A writer discusses the use of pepsin and quotes a number of eminent authorities who appear to agree that pepsin is rarely indicated and that the best therapy, in functional disorders of the stomach, is obtained by a stimulation of the function of the stomach rather than

by a useless or even successful attempt at their substitution.—J. Am. M. Ass., 1905, v. 45, p. 1441.

Schwarz, Osw., elaborates on the work done by Pollack on the antiferment of trypsin and recounts some experiments that he has made with pepsin. He finds that on heating a pepsin solution an inhibiting body is liberated. This inhibiting body, or antipectin, he believes to be present normally in pepsin.—Chem. Centralbl., 1905, v. 76, p. 341 (from Beiträge z. chem. Physiol. u. Pathol., 1905, v. 6, pp. 524–542).

PETROLATUM.

van der Wielen, P., proposes the following formula for a petrolatum compound that is said to be capable of taking up and holding as much as 75 per cent of water or of aqueous solutions, and should, therefore, be used as an ointment base. For a white cerate he suggests 5 parts of white wax and 95 parts of white petrolatum and for the yellow cerate a corresponding quantity of yellow wax and petrolatum.—Pharm. Ztg., Berlin, 1905, v. 50, p. 552.

PETROLATUM LIQUIDUM.

Vanderkleed, Charles E., points out that all qualities of liquid petrolatum are to be had on the market and that pure goods can readily be obtained by paying the right price. The presence of traces of free acid and of sulphates should be guarded against.—Proc. Pennsylvania Pharm. Ass., 1905, p. 55.

PHENOL.

Lyons, A. B., points out that there is an inconsistency between the statement of solubility, in water, of phenol and of liquified phenol.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 260.

Riedel's Berichte points out that Schmidt, Beilstein, Kahlbaum, and other investigators give figures, for the boiling point of phenol, that range from 182 to 184.1° C., and the experiments recorded in Riedel's Berichte appear to indicate that the upper limit, 182°, of the pharmacopœia is too low.—Riedel's Berichte, 1905, p. 42.

Vanderkleed, Charles E., calls attention to the possibility of the 95 per cent "carbolic acid solution" of the chemical manufacturer may contain only 91.2 per cent of absolute phenol.—Proc. Pennsylvania Pharm. Ass., 1905, p. 193.

Lloyd, S. J., presents an exhaustive study of the attempts to devise a satisfactory method for the quantitative estimation of phenol. He presents a record of his analyses and some suggestions on the conditions under which phenol can be accurately determined.—J. Am. Chem. Soc., 1905, v. 27, pp. 16–24.

An abstract (from *J. de Pharm. d'Anvers*, 1905, p. 150) outlines a method for determining phenol by the addition of an excess of bromine and titrating this back with iodine and thiosulphate. To avoid the uncertainty of the end reaction the author recommends dissolving the precipitate in 1 cc. of chloroform.—*Pharm. Zentralh.*, 1905, v. 46, p. 531.

Moerk notes that by the usual method (precipitating with an excess of bromine solution and titrating with thiosulphate) the precipitated tribromophenol obscures the end reaction. He recommends the use of chloroform to dissolve the precipitate and thus increase the delicacy of the test.—*Proc. Maryland Pharm. Ass.*, 1905, p. 66.

Reuter, L., ascribes the reddening of phenol to oxidation and suggests preventing this by the addition of a small quantity of sulphurous acid.—*Schweiz. Wehnschr. f. Chem. u. Pharm.*, 1905, v. 43, p. 355.

Arnold and Werner outline a number of tests for differentiating between phenol and cresol.—*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 925.

An editorial based on an article in the *Pharmaceutical Journal* contains some general descriptive data concerning phenol.—*Am. Druggist*, 1905, v. 47, p. 7.

Swisher, T. J., reports the successful, though late, use of alcohol to counteract the local caustic effect of phenol.—*J. Am. M. Ass.*, 1905, v. 45, p. 717.

v. Chlumsky (*Zentralbl. f. Chir.* 1905) recommends the use of a mixture of phenol, 30; camphor, 60; and alcohol 10.—*Apoth. Ztg.*, Berlin, 1905, v. 20, p. 727.

PHENYLIS SALICYLAS.

Herting, Otto, discusses the nomenclature, tests, composition, and the method of making phenyl salicylate.—*Deut.-Amer. Apoth. Ztg.*, 1905, v. 26, p. 113.

PHOSPHORUS.

Christomanos, A. C., discusses the estimation of the solubility of ordinary yellow phosphorus in ether and benzol. 100 gms. of ether at 0° C. dissolved 0.4335 gm. of phosphorus, and at the boiling point of the solvent, 35° C. 1.9984 gms. 100 gms. of benzol dissolves 1.513 gms. of phosphorus at 0° C., and 10.027 gms. at 81° C.—*Ztschr. f. anorgan. Chem.* 1905, v. 45, pp. 132–141.

Enell, Henrik, discusses the quantitative estimation of phosphorus in phosphorated oil.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 601; see also *Svensk. Pharm. Tidskr.* 1905, v. 9, pp. 229–236.

Rupp, E., discusses the above method and points out that the results are not uniformly reliable.—*Pharm. Ztg.*, 1905, v. 50, p. 621.

PHYSOSTIGMA.

Hartwich, C., describes a bean, not at all resembling physostigma, that had been sent to Hamburg as physostigma. He explains this by pointing out that a number of more or less similar beans are known in Africa as "Garbee" and that this particular bean, known to the natives as Opochala, Owala, and Orvala, is also sometimes called "Calibohnen."—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 677 (from Schweiz. Wehnschr. f. Chem. u. Pharm.).

An abstract points out that the false calabar bean, found on the Hamburg drug market, according to Schinz is a seed of *Pentaklethra macrophylla*, Benth., a leguminous tree indigenous to tropical Africa.—*Ibid.*, p. 751.

Vanderkleed, Charles E., reports five assays of physostigma which varied from 0.148 to 0.446 per cent of alkaloid.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 55.

Naylor, W. A. H., points out that the most recent investigations indicate the presence of three bases, eserine, eseridine, and eseramine, while the nonexistence of calabarine can no longer be a matter of doubt. Eserine is supposed to represent the therapeutic properties, on which the physician depends when he prescribes the official extract, and as commercial extracts of the bean, made with rectified spirit, have been shown by MacEwan to contain from 1 to 10 per cent of total alkaloid, this fact may be adduced as being of sufficient importance to indicate the need for standardizing the extract of this drug.—*Pharm. J.*, Lond., 1905, v. 21, p. 126.

Maben, Thomas, points out that the standard for the solid extract of physostigma, 2 per cent, indicates that it is thirteen times stronger than the bean, but even so, it is still much below the figure found in the extract.—*Pharm. J.*, Lond., 1905, v. 21, p. 141.

Beckurts, H., reports some work done on the assay of physostigma and extract of physostigma in the pharmaceutical institute of the technical high school of Brunswick, by Köhler and Frerichs, which further demonstrates the usefulness of iodeosin as an indicator in the titration of the alkaloids of physostigma. In the preliminary treatment, Beckurts prefers to use a 10 per cent solution of potassium bicarbonate in place of the sodium bicarbonate, as directed in the U. S. P., VIII.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 670.

Douglass, Malcolm E., outlines the use of physostigma in eye affections, torpor of the intestines, convulsive disorders, etc.—*Hahne-man. Month.*, Phila., 1905, v. 40, p. 852.

PHYSOSTIGMINÆ SALICYLAS.

Huebner, W., discusses the chemistry and the pharmacology of physostigmine. In connection with the constitution of physostig-

mine, he proposes a structural formula, and points out that physostigmine decomposes into eserolin and rubreserin. He also reviews the reported pharmacologic action of physostigmine, and reports on a number of experiments, which serve to demonstrate that the organism is not accustomed to the drug, and that the poison is at least partially eliminated through the urine.—Arch. f. exper. Path. u. Pharmacol., 1905, v. 53, pp. 313-330.

PHYTOLACCA.

Eberle, E. G., mentions *Phytolacca decandra* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Lloyd, John Uri, points out that the question of quality, by reason of insect attack and age, is all important with this drug.—Pharm. Rev., 1905, v. 23, p. 331.

PILOCARPINÆ HYDROCHLORIDUM.

Siedler, P., believes that the melting point for pilocarpine hydrochloride given in the Ph. Germ., IV (193-195° C.), is rather low. He found it to require 196.5°, and in an air bath as much as 199° C.—Pharm. Post, Wien, 1905, v. 36, p. 568.

Jowett, H. A. D., discusses the constitution of pilocarpine and the conversion of iso-pilocarpine into pilocarpine. He controverts the views expressed by Pinner that the isomerism is not solely stereochemical, but structural.—Abstr. in Chem. News, Lond., 1905, v. 91, p. 268.

Pinner, Adolf, presents an exhaustive study of the constitution of certain derivatives of pilocarpine, and of iso-pilocarpine.—Abstr. in J. Chem. Soc., Lond., 1905, v. 88, part 2, pp. 463-465 (from Ber. d. deut. chem. Gesellsch., 1905, v. 38, pp. 1510-1531).

MacCallum, J. B., discusses the action of pilocarpine on the flow of urine.—(Univ. Calif. Pub. Physiol., Berkeley, 1905, v. 2, pp. 105-112.) Reference from Ind. Med., 1905, p. 675.

PILOCARPUS.

Rusby, H. H., points out that pilocarpus is a drug of great power, yet a majority of the drug sold is nearly inert. He states that a large manufacturing house was habitually using the spurious article.—Merck's Rep., 1905, v. 14, p. 212.

Dohme, A. R. L., points out that, up to 1901, jaborandi ran low in alkaloids, but that since then it has run up to and even higher than 1 per cent. The laboratory report shows a variation of from 0.19 per cent in 1899 and 0.23 per cent in 1900 to 1.2 per cent in 1904 and 1905.—Apothecary, Boston, 1905, v. 17, p. 942.

Maben, Thomas, points out that so long as the U. S. P., VIII, recognizes both the nitrate and the hydrochloride of pilocarpine it seems a pity that this alkaloid should not also have been made the basis of the standard for the drug in place of "alkaloids mainly pilocarpine," the actual composition of which may vary to a greater or less degree.—Pharm. J., Lond., 1905, v. 21, p. 141.

Naylor, W. A. H., points out that the inference to be drawn from Jowett's chemical investigation and Marshall's physiological experiments is that the preparations of jaborandi should be assayed for pilocarpine and not for total alkaloid, and, further, that inasmuch as pilocarpine possesses acid properties the fixed alkalies should not be used in connection with "shake-out solvents." He also asserts that he knows of no process which is capable of determining within 5 per cent the amount of pilocarpine present in a preparation of pilocarpus.—Pharm. J., Lond., 1905, v. 21, p. 126.

Umney (Pharm. J., Lond.) asserts that *Pilocarpus jaborandi* never contains more than 0.5 per cent of total alkaloids, of which not more than one-half is pilocarpine. *Pilocarpus macrophyllus*, on the other hand, contains 0.8 per cent of total alkaloids, or from 0.35 to 0.5 per cent of pilocarpine.—Pharm. Zentralh., 1905, v. 46, p. 670.

Weigel (Pharm. Zentralh.) reports examining a sample of Guadeloupe jaborandi received from Marseille. He notes the remarkable size of the leaf and the prominent midrib. Weigel obtained 0.353 per cent of alkaloid; other observers have found as high as 1.0 per cent.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 314.

Caeser and Loretz recommend the determination of the moisture content and an assay for alkaloids. For the latter they outline a process that is similar to that in the U. S. P., VIII, using in place of complete exhaustion an aliquot part of the solution. They also outline a method for the titrimetric estimation of the alkaloid. G. Fromme recommends washing out any excess of chlorophyll that may be present in the aqueous acid solution with ether. This, he declares, will facilitate the final determination, gravimetrically as well as titrimetrically.—Geschäfts-Ber. v. Caeser & Loretz, in Halle a. S., 1905, pp. 4 and 88.

PILULÆ.

An abstract or unsigned article gives directions for coating pills with salol.—Western Druggist, 1905, v. 27, p. 447.

PILULÆ FERRI CARBONATIS.

In the column on pharmacology there is an interesting comment on "Scientific work misrepresented and commercialized," which includes some references on the comparative value of Bland's pills.—J. Am. M. Ass., Chicago, 1905, v. 45, p. 934.

PIMENTA.

Spaeth, E., points out that among the more common forms of adulteration are the addition of cacao hulls to powdered pimenta, the coloring of damaged pimenta and the treatment of inferior qualities with solution of resin. Pimenta should not be wholly or partially extracted, should not contain more than 2 per cent of stems and should contain no overripe, black, or soft fruit. The ash should not exceed 6 per cent, and the amount that is insoluble in 10 per cent hydrochloric acid should not exceed 0.5 per cent. Pimenta should contain at least 2 per cent of ethereal oil.—Ztschr. f. Nahr. u. Genussm., Berlin, 1905, v. 10, p. 30.

Roxburgh, A., gives directions for growing *Pimenta officinalis* in Jamaica, and points out that the average production of that drug is placed at from 50,000 to 60,000 bags of 150 pounds each.—Exp. Sta. Rec., v. 17, p. 769 (from Agr. News, Barbadoes, 1905, v. 4, p. 295.)

PIPER.

Winton and Bailey present a comprehensive study of Lampong, Acheen, and Penang pepper with a complete report of their findings.—Rep. of the Conn. Exper. Sta. Abstracted in Ztschr. f. Unters. d. Nahr. u. Genussm., Berlin, 1905, v. 9, p. 227.

Hoton, L., reports on the ash and the sulphuric acid residue found in black pepper. His report includes a table giving percentages of ash, mineral matter, sulphuric acid residue, alcoholic extract, and the price of a number of samples of black pepper, including Aleppi, Tellicherry, Lampong, and Penang.—J. de Pharm. d'Anvers, 1905, v. 61, pp. 201–212.

Spaeth, Eduard, presents a didactic discussion on the adulteration of black pepper, the substances used as adulterants and the several methods suggested for the detection of these adulterations.—Ztschr. f. Unters. d. Nahr. u. Genussm., 1905, v. 9, pp. 577–595.

Spaeth, E., is inclined to think that 7 per cent of ash for whole pepper is rather high. He has met with a ground pepper which contained as much as 50 per cent of added pepper hulls and which yielded only 6.5 per cent of ash. The amount of ash insoluble in 10 per cent of hydrochloric acid should not exceed 2 per cent. For white pepper the total amount of ash should not exceed 4 per cent, and the amount insoluble in 10 per cent hydrochloric acid should not exceed 1 per cent. *Ibid.*, v. 10, p. 27.

Kebler, Lyman F., reports finding pepper adulterated with tapioca colored black with lampblack.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 188.

Dachs (J. de Pharm. d'Anvers) reports finding a sample of powdered white pepper containing upwards of 20 per cent of a starch-

like substance.—*Ztschr. f. Unters. d. Nahr. u. Genussm.*, 1905, v. 9, p. 229.

Jean, F. (*Ann. de Chim. analyt.* v. 9, pp. 423–425), describes two powders that closely resemble black and white pepper and are being sold in France under the respective names of *Le Griffon* and *Le Mito*. These powders are stated to consist of vetch, popularly known as “*Chère aux pigeons*,” and are thus very similar to the pepper substitute sold as *Erviop* (*Analyst*, v. 29, p. 309).—*Analyst*, London, 1905, v. 30, p. 22.

PIPERINA.

Reichard reviews the reactions and tests that have been proposed for piperine and presents a study of the behavior of this alkaloid with a number of well-known reagents.—*Pharm. Zentralh.*, 1905, v. 46, p. 935.

PIX LIQUIDA.

An editorial characterizes the syrup of tar as a relic of barbarism that would not have been missed from the pharmacopœia.—*Drug Topics*, N. Y., 1905, v. 20, p. 216.

PLUMBUM.

Dittrich and Reise (*Berichte*, 1905, v. 38, pp. 1829–1831) discuss the determination of lead by persulphate in acid solution, and believe that this mode of precipitation is much more rapid than the usual precipitation by sulphuric acid and alcohol, and is equally accurate. No other metals are carried down with the lead.—*Abstr. in J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 691.

Belton, F. G. (*Chem. News*, 1905, v. 91, p. 191), points out that the determination of lead as sulphate, in the presence of potassium salts, often leads to too high results, due to the formation of a lead potassium sulphate. He recommends that the precipitation of the lead as sulphate should take place at boiling heat, and that excess of sulphuric acid should be used.—*Abstr., Ibid.*, p. 561.

PLUMBI ACETAS.

Patch, Edgar L., reports finding lead acetate badly carbonated. He found none that corresponded perfectly with the U. S. P., VIII. *Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 185.

PLUMBI OXIDUM.

An abstract from the Helffenberger *Annalen* points out that of eight samples of lead oxide examined six complied with the requirements of the German Pharmacopœia. Seven of the samples con-

tained traces of iron and one of them contained a considerable quantity.—Südd. Apoth. Ztg., 1905, v. 45, p. 521.

PODOPHYLLUM.

Lloyd, John Uri, asserts that this drug is so cheap and so characteristic as to forbid intentional adulteration, and yet it is often contaminated with foreign roots. The most serious difficulty in connection with podophyllum is that of its being collected in the spring, when the root is comparatively worthless, instead of in the fall after the top has dried.—Pharm. Rev., 1905, v. 23, p. 331.

Watkins, in discussing the uses of podophyllum, says: "It is indicated by a full face, full, oppressed pulse, full, dirty, yellowish coated tongue, dizziness, floating specks before the eyes and mental dullness.—Eclectic Med. J., 1905, v. 65, p. 684.

Kinyon, H. E., points out that podophyllum is indicated in diseases of the liver which decrease or prevent the flow of biliary secretions.—Hahnemann. Month., Phila., 1905, v. 40, p. 795.

POTASSII BITARTRAS.

Voignier, Paul (Rev. de Chim., Ind.), outlines the process used to purify lees and tartar, gives an account of the crude material, the source from which it is obtained, the analysis of the crude material, and discusses the employment of bitartrate of potassium for standardizing acid and alkaline liquids.—Paint, Oil and Drug Rep., 1905, Aug. 21, p. 24.

Wetterstroem, Theo. D., reports examining 3 samples of potassium bitartrate, all impure, 97.2, 98.5 and 98.8 per cent pure.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 184.

Lowry, W. J., reports finding one sample of potassium bitartrate which was not soluble to the proper degree and which contained chlorides, sulphates, and calcium.—Proc. Maryland Pharm. Ass., 1905, pp. 49-50.

Havenhill, L. D., reports finding a number of "grocers" samples of potassium bitartrate that were exceedingly variable as to quality and price. The chief adulterant was commercial acid phosphate of calcium.—Proc. Kansas Pharm. Ass., 1905, p. 92.

Millard, E. J. (Chem & Drugg., v. 65, p. 399), reports finding a considerable proportion of maize starch in potassium bitartrate.—Year Book of Pharmacy, Lond., 1905, p. 70.

Perry, Ernest J., considers a colorimetric process the best for the detection of lead, copper, and iron in potassium bitartrate, and commends the process of Warrington as being most reliable. For the actual estimation of the amount of true acid tartrate, he believes that the Ph. Brit., 1898, method is liable to error and suggests a better

method; also suggests a method for the estimation of the sulphate of calcium.—*Chem. & Drug.*, Lond., 1905, v. 67, p. 838.

POTASSII BROMIDUM.

Caspari, Charles E., reports that of 25 samples of potassium bromide examined, 14 answered the requirements of the U. S. P., three contained an excess of potassium chloride, two contained potassium sulphate, one contained sodium, and five contained dirt mechanically held.—*Proc. Missouri Pharm. Ass.*, 1905, p. 74.

The committee on adulteration reports that of six samples examined, three answered the requirements of the U. S. P.; one was quite dirty, one contained potassium sulphate, and two an excess of potassium chloride.—*Proc. Michigan Pharm. Ass.*, 1905, p. 79.

Havenhill, L. D., reports finding one sample of potassium bromide containing an excessive amount of sulphates.—*Proc. Kansas Pharm. Ass.*, 1905, p. 92.

Meusser, A., discusses the solubility of potassium chloride, bromide, and iodide in water, both above and below 0° C.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 275 (from *Ztschr. f. anorgan. Chem.*, 1905, v. 44, pp. 79–80).

POTASSII CARBONAS.

Kebler, L. F., in discussing the testing of chemical reagents, points out that with one exception all of the samples of potassium carbonate were reported to contain either chloride or sulphate, or both. The fact that one sample was free from these contaminations is pointed out as being evidence that a pure article can be produced.—*Proc. Ass. Off. Agr. Chem.*, 22 Ann. Conv., p. 186.

POTASSII CHLORAS.

Ditz, Hugo, discusses the action of concentrated hydrochloric acid on potassium chlorate in the presence of potassium iodide or bromide.—*Ztschr. f. angew. Chem.*, 1905, v. 18, pp. 1516–1520.

Davidson, E., has examined the decomposition of potassium chlorate, by hydrochloric acid, in dilute solutions, taking every precaution to exclude air, and determining after varying intervals of time the amount of chlorine set free.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 844 (from *Ztschr. f. angew. Chem.*).

POTASSII CITRAS.

Kebler, Lyman F., reports a sample of potassium citrate as being off color, and containing mechanical impurities, chloride, and sulphate.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

POTASSII CYANIDUM.

Kebler, Lyman F., reports finding two samples of potassium cyanide; one labeled "Reagent," contained 94.6 per cent of potassium cyanide, the balance largely chloride; and another, labeled "C. P.," contained but 89.64 per cent of the pure chemical.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

Jollyman, W. H., reports being able to detect the presence of potassium cyanide some time after the death of the animal, thus demonstrating the resistance of potassium cyanide during decomposition.—*Apoth. Ztg.*, Berlin, 1905, p. 972, v. 20 (from *Ann. de Chim. analyt.*).

POTASSII HYDROXIDUM.

Kebler, Lyman F., reports finding a sample of potassium hydroxide labeled "Strictly C. P. (free from sulphur)" which contained sulphate and chloride.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

Thiele and Marc outline the preparation of a stable alcoholic potash solution prepared by decomposing potassium sulphate with barium hydroxide and dissolving the resulting potassium hydrate in alcohol.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 103 (from *Ztsch. f. öffentl. Chem.*).

Haupt suggests that a permanently colorless alcoholic solution of potassium hydroxide can be prepared by dissolving 35 gm. of potassium hydroxide in sticks in 100 cc. of absolute alcohol, removing the insoluble carbonate and diluting the resulting solution with 90 per cent alcohol to the desired concentration. $\frac{1}{2}$ N. solution will remain colorless for months at a time.—*Pharm. Zentralh.*, 1905, v. 46, p. 569.

Alvarez, E. P., asserts that a 5 per cent solution of eikonogen or sodium amino-naphthol-sulphonate is a more delicate reagent for potassium in neutral solutions of potassium salts than is platinic chloride.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 637 (from *Compt. rend.*, 1905, v. 140, pp. 1186–1187).

POTASSIUM IODIDI.

Caspari, Charles E., examined forty samples of potassium iodide, only ten of which answered all of the tests of the U. S. P. Five contained an excess of alkali, five contained sodium, ten samples contained sulphate, nitrate, and chloride, and in twelve samples small quantities of iodate were found.—*Proc. Missouri Pharm. Ass.*, 1905, p. 74.

The committee on adulteration examined eight samples of potassium iodide, only two of which answered all of the requirements of the U. S. P. Two samples had a small amount of iodate, three had sulphates and chlorides, and one had an excess of alkali.—*Proc. Michigan Pharm. Ass.*, 1905, p. 79.

Patch, Edgar L., reports finding a sample of potassium iodide containing an excess of iodate, free iodine, and iron.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

Meusser, A., discusses the solubility of potassium iodide, bromide, and chloride in water and presents a chart and a table giving their solubility at different temperatures.—*Ztschr. f. anorgan. Chem.*, 1905, v. 44, pp. 79–80.

Torrey and Hunter discuss the action of potassium iodide on acetone solutions of bromanil and chloranil.—*Ber. d. deut. chem. Gesellsch.*, 1905, v. 38, pp. 555–556.

POTASSII NITRAS.

Hooper, D., discusses the process of nitrification with special reference to the conditions obtaining in India. He gives some account of the districts where nitre earths occur and where the salt is manufactured, describes the process of manufacture and gives a series of assays of samples of nitre earths, crude and refined saltpetre, and impure and purified table salt and other by-products.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 1170.

Kebler, Lyman F., reports finding a sample of potassium nitrate labeled "C. P." which contained but 86.3 per cent of pure potassium nitrate.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

Bensemam, R., makes a contribution to the analysis of potassium nitrate, discusses the practicability of converting the nitrate into carbonate by the addition of oxalic acid, displace the liberated nitric acid and finally heat to convert the oxalate into carbonate. The resulting carbonate is then determined by titration.—*Ztschr. f. angew. Chem.* 1905, v. 18, p. 816.

For some additional notes directing attention to methods for estimating the impurities in Chile saltpetre, see *Ibid.*, p. 939, also p. 1225.

POTASSII PERMANGANAS.

Kebler, Lyman F., in discussing chemical reagents, points out that potassium permanganate usually contains chloride or sulphate or both. Inasmuch as it frequently serves as the basis in the preparation of standard volumetric solutions every possible care should be exercised to secure a pure article. A number of samples examined show that arsenic is by no means an uncommon impurity.—*Proc. Off. Agric. Chem.*, 22 Ann. Conv., p. 186.

Gawalowski, A., describes several interesting reactions of potassium manganate and permanganate which appear to possess practical value. Among other reactions it is pointed out that the addition of metallic mercury to an alkaline permanganate results in the gradual production of a violet blue compound.—*Merck's Rep.*, N. Y. 1905, v. 14, p. 281.

Friend, J. A. N. (Proc. Chem. Soc., 1905, v. 21, p. 133), outlines a process for the estimation of potassium permanganate in the presence of potassium persulphate.—Pharm. Ztg., Berlin, 1905, v. 50, p. 603.

Gardner and North have made a series of experiments with solutions of potassium permanganate and of ammonium oxalate and conclude that solutions of the former when made with pure ingredients are stable and will readily keep for at least twelve months without deterioration.—Abstr. in Deut.-Amer. Apoth. Ztg., N. Y., 1905, v. 26, p. 17.

Lemaire (Répert. de Pharm.) has experimented with a number of nonoxidizable substances that might be of use for the making of caustic points of potassium permanganate. He finds that sodium phosphate, containing about 12 molecules of water, melts at 40° C. and answers admirably for the production of points by moulding them in suppository moulds.—Pharm. Zentralh., 1905, v. 46, p. 861.

An abstract (from Münch. Med. Wchnschr.) recommends a mixture of 2 parts of potassium permanganate, 1 part of kieselguhr and 1 part of paraffin ointment as a hæmostatic, to be used in minor operations, nose bleed and similar cases.—Pharm. Ztg., Berlin, 1905, v. 50, p. 804.

POTASSII ET SODII TARTRAS.

Kebler, Lyman F., reports finding potassium and sodium tartrate that was very dirty and contained iron salt and chloride.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 189.

Meredith, H. L., reports on a sample of potassium and sodium tartrate which analysed from 55–57 per cent of potassium and sodium tartrate, the remainder a very inferior sodium bicarbonate.—Proc. Maryland Pharm. Ass., 1905, p. 55.

PRUNUM.

Eberle, E. G., mentions *Prunus domestica* and *serotina* as occurring in Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

PRUNUS VIRGINIANA.

Havenhill, L. D., points out that lack of conformity to degree of fineness of powder specified is accountable for the reported difficulties in percolating wild cherry and the lack of uniformity of preparations.—Proc. Kansas Pharm. Ass., 1905, p. 93.

PULVIS GLYCYRRHIZÆ COMPOSITUS.

Evans, J. (Pharm. J., Lond.), gives tabulated results of examinations of 5 samples, including amount of ash and the alcohol soluble extract.—Year Book of Pharmacy, Lond., 1905, p. 267.

PULVIS IPECACUANHÆ ET OPII.

The Ph. Hisp., VII, includes this preparation under the title "Pulvis ipecacuanhæ opiatus," and directs it to be made from 10 parts each of powdered ipecacuanha and powdered opium with 40 parts each of powdered potassium nitrate and potassium sulphate. The several ingredients are to be thoroughly triturated in a mortar until a homogeneous mixture results.—*Farmacopea Official Española*, 1905, p. 484.

QUERCUS.

Eberle, E. G., mentions *Quercus alba* among the medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 305.

QUININA.

Murray, Benjamin L., discusses the structural formula of quinine and presents a chronological bibliography, comprising 68 references, on the constitution of quinine and related compounds.—*Merck's Rep.* N. Y., 1905, v. 14, p. 301.

Lyons, A. B., points out that the several tests for the purity of the different quinine salts are still open to the very serious objection that the same weight of the salt is taken in each case without regard to the percentage of quinine in the salt. The test is therefore relatively more stringent in the case of quinine alkaloid than it is in the case of quinine bisulphate. The inconsistency of this was pointed out long ago by Dr. Prescott and has been commented upon by others, so that the Revision Committee sinned not from ignorance. He also points out that the proposition to substitute lime water for ammonia water should be investigated, and doubts if there is any good reason for embarrassing the assay with the time consuming detail of drying "for two hours at 50° C."—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 259.

The report of the Bandeong quinine factory for 1904 shows that 921,317 kilos of bark have been worked during the year, containing, according to analysis, a total of 56,210.34 kilos of cinchona alkaloids, which, after deduction of waste, yielded 54,616.66 kilos. The Dutch Indian Government has contracted for from 15,000 to 20,000 kilos of quinine sulphate this year.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, p. 1135 (from *Chem. and Drugg.*).

An editorial calls attention to the passing of quinine, as evidenced by the marked decline in the amount of quinine used within the past year.—*Am. Druggist*, 1905, v. 47, p. 198.

Reichard, C., discusses the reactions of quinine and cinchonine with a number of substances, such as mercurous nitrate, copper oxychloride, ammonium persulphate, potassium dichromate, sulphuric acid with ammonium molybdate, etc.—*Pharm. Ztg., Berlin*, 1905, v. 50, p. 314.

Battandier, J. B., discusses the color reactions for quinine and quinidine.—Year Book of Pharmacy, Lond., 1905, p. 136 (from J. Pharm. Chim.).

Robertson, P. W., outlines a method for the estimation of quinine and cinchona alkaloids depending on the use of ammonium sulphocyanide and a zinc or mercury salt.—Australas. J. Pharm., 1905, v. 20, pp. 101-102.

Guiges, P., presents a study of the action of ammonia and its salts on the crystallization of the salts of quinine.—J. de Pharm. et de Chim., Paris, 1905, v. 22, p. 299.

Yvon produces a tasteless quinine mixture by mixing a small quantity of sodium bicarbonate with quinine, and sufficient oil of almonds to form a paste. The resulting mixture may be flavored by adding a trace of oil of lemon, or oil of peppermint. The sodium bicarbonate is said to neutralize the acids present in the mouth and thus prevent solution.—Pharm. Ztg., Berlin, 1905, v. 50, p. 663.

Lacroix, H., gives a method for preparing and some description of the properties of quinine formiate.—J. de Pharm. et de Chim., 1905, v. 22, p. 99.

Allen reports finding quinine capsules that were not true to the claims made for them.—Proc. Michigan Pharm. Ass., 1905, p. 80.

Ramsay, E. T., discusses the use of quinine in pneumonia.—Abstr. in J. Am. M. Ass., 1905, v. 45, p. 1447 (from Virginia M. Semi-Month.).

Nieder, Charles F., reports his observations in connection with several cases of pneumonia treated with quinine and iron.—J. Am. M. Ass., 1905, v. 45, p. 1572.

QUININÆ BISULPHAS.

Gane, E. H., reports finding a sample of quinine bisulphate containing 1.7 per cent of potassium sulphate.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 188.

QUININÆ HYDROCHLORIDUM.

Carette, M. H., discusses the composition of neutral hydrochloride of quinine and the variation in composition when crystallized from different solvents.—J. de Pharm. et de Chim., Paris, 1905, v. 22, p. 299.

Erba, Carlo, calls attention to his study of the composition of neutral hydrochloride of quinine (Boll. Farm., 1901). According to his observations the salt crystallized from 95 per cent alcohol is hydrated and has the formula $C_{20}H_{24}O_2N_2HCl \cdot C_6H_5OH \cdot H_2O$, whilst Carette states that it contained 1.5 molecules of water.—J. Chem. Soc., Lond., 1905, part 2, p. 151 (from J. Pharm. Chim.).

Garsed, William, believes that his experiments go to show (1) that the quinine acid hydrochloride of commerce is practically an anhydrous salt and does not contain the three molecules of water given in the pharmacopœial formula. (2) That the pharmacopœial (Brit.) tests for the presence of neutral chloride should be more precise, both maximum and minimum figures being given, with particular instructions as to the indicator to be used.—*Pharm. J., Lond.*, 1905, v. 21, p. 138.

QUININÆ SULPHAS.

Paul, B. H., discusses the testing of quinine sulphate for cinchonidine, based upon the solubility of quinine and cinchonidine in ether and the influence of the presence of the latter on the solubility of the former.—*Year Book of Pharmacy, Lond.*, 1905, p. 142 (from *Chem. & Drug.*, v. 65, p. 428).

Patch, Edgar L., reports finding an excess of other alkaloids in quinine sulphate, and quinine pills containing only 1.3 grains of quinine in place of 2 grains.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

RESINA.

Levy, Paul, discusses the structural formula proposed for abietinic acid, the chief constituent of American rosin. He concludes that the formula proposed by Tschirch, Bagley and others can not be correct and that the formula proposed by Trommsdorf, $C_{40}H_{60}O_4$, is probably correct though he believes that it may correctly be represented by the more simple formula: $C_{20}H_{30}O_2$.—*Ztschr. f. angew. Chem.*, 1905, v. 18, pp. 1738-1741.

Tschirch, A., presents a study of the various phenomena inducing or tending to induce the flow of resins.—*Arch. d. Pharm.*, 1905, v. 243, p. 81.

RESINA PODOPHYLLI.

Patch, Edgar L., reports on five samples of resin of podophyllum which contained, respectively, 3, 5, 2.5, 5.5, and 2.5 per cent of material insoluble in alcohol.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 188.

The committee on adulteration of the N. W. D. A. quotes from a communication that podophyllin sold in a large way is frequently adulterated, and reference is made to a report on one sample which was found to contain between 30 and 40 per cent of aloin. Other samples have been found mixed with gamboge in various proportions.—*Paint, Oil and Drug Rep.*, 1905, Oct. 6, p. 15.

The report of inspectors of pharmacies in Belgium asserts that resin of podophyllum is rarely pure; certain samples were found to

contain as high as 15 per cent of material insoluble in alcohol and 18 per cent of matter insoluble in ammonia.—Bull. Soc. Roy. de Pharm. de Bruxelles, 1905, v. 49, p. 303.

RESINA SCAMMONII.

Guiges, P., calls attention to the unsatisfactory nature of the ether test for scammony resin and points out that much of the scammony of commerce is made from *Ipomœa orizabensis*, the so-called American scammony.—J. de Pharm. et de Chim., Paris, 1905, v. 22, p. 241.

RESORCINOL.

Kaiser, Sigism., reports the observations made in connection with a case of lupus in which a 50 per cent resorcin ointment had been used with nearly fatal result.—Apoth. Ztg., Berlin, 1905, v. 20, p. 656 (from Berl. Klin. Wchnschr., 1905, v. 42, p. 1039).

RHAMNUS PURSHIANA.

Eberle, E. G., mentions *Rhamnus purshiana* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

True, Rodney H., says that *Rhamnus purshiana* is grown at Washington, D. C., as seedlings of different ages, and as young transplanted trees shipped from the State of Washington.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 275.

Zeig, A. C., presents an exhaustive account of the introduction, method of collecting and marketing of cascara sagrada.—Pharm. Era, 1905, v. 34, p. 150.

Groff, John E., in a paper written for the Lewis and Clark Pharmaceutical Congress, presents a collection of interesting facts relating to the history, pharmacognosy, chemical composition, and pharmacology of cascara sagrada.—Am. Druggist, N. Y., 1905, v. 47, p. 264.

Brown, J. Lee, describes the methods employed in gathering, peeling, drying, breaking, packing, and marketing cascara bark.—Western Druggist, 1905, v. 27, p. 701.

Vanderkleed, Charles E., outlines a method for the assay of emodin-yielding drugs.—Proc. Pennsylvania Pharm. Ass., 1905, p. 193.

Panchaud, Adalb., has repeatedly found but 0.5 per cent of emodin in the fluid extract of *Rhamnus purshiana*. He also believes that the addition of magnesia to the drug, before percolating, to remove or to modify the bitter principle, tends to unite with a portion of the emodin and make it insoluble in the prescribed menstruum. He recommends a menstruum containing at least 50 per cent of alcohol.—Schweiz. Wchnschr. f. Chem. u. Pharm., 1905, v. 43, p. 520.

Warin, M. J., presents a comparative study of the oxymethylantraquinone content of frangula and cascara sagrada, and of their respective fluid extracts. He found that a comparatively larger proportionate amount of the contained oxymethylantraquinone was extracted in the making of fluid extract of cascara sagrada than in the making of fluid extract of frangula.—*J. de Pharm. et de Chim.*, Paris, 1905, v. 22, p. 12.

Thurston, Azor, reports the determination of the alkalinity of the water-soluble ash in 9 samples of the leading brands of fluid extract of cascara sagrada. The number of cc. of $\frac{1}{10}$ N. acid required to neutralize the water-soluble ash from 100 gm. of sample varied from 59.2 to 97.7.—*Proc. Ohio Pharm. Ass.*, 1905, p. 34.

Gadd, H. Wippell and Sydney C., propose that 110 minims of a liquid extract of cascara sagrada evaporated over a water bath for four hours should yield not less than 20 grains of extract.—*Pharm. J.*, Lond., 1905, v. 21, p. 579.

An editorial expresses some doubt as to whether or not the aromatic fluid extract of cascara sagrada will become popular, as the public has become accustomed to the wintergreen-sassafras combination.—*Drug Topics*, N. Y., 1905, v. 20, p. 213.

RHEUM.

Gilson, E., presents a comprehensive review of the history and of our general knowledge of rhubarb, and reports some experimental work to determine the active principles of Chinese rhubarb.—*Arch. internat. de Pharmacod. et de Thérap.*, 1905, v. 14, pp. 455–503.

Vanderkleed, Charles E., outlines a method for the assay of emodin-yielding drugs.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 193.

Tschirch, A. (*Pharm. Zentralh.*, v. 45, p. 496), has devised a method for the colorimetric valuation of rhubarb, which consists in the hydrolysis of the anthraglucosides of rhubarb and the solubility of the resulting oxymethylantraquinone in ether.—*Analyst*, Lond., 1905, v. 30, p. 60.

Tschirch, A. (*Schweiz. Wehnschr. f. Chem. u. Pharm.*, v. 43, p. 253), describes a ready method for detecting the admixture of *Rheum rhaponticum* in other varieties of the drug. This method depends on the insolubility in ether of the crystalline principle rhaponticin or ponticin.—*Pharm. J.*, Lond., 1905, v. 21, p. 97.

Tschirch and Cristofolletti present a short review of the work previously done on the root of *Rheum rhaponticum*, and a report of an exhaustive study of the composition of roots grown in Austria and in Berne, Switzerland.—*Arch. d. Pharm.*, Berlin, 1905, v. 243, p. 443.

An abstract from the annual report of Philip Roeder points out that, in addition to the macroscopic and microscopic characteristics,

much weight is to be given to the amount of aqueous extract and to the ash content. The maximum proposed by Hauke (*Zeit. d. allg. oestr. Apoth. Ver.*, 1902), 13 per cent, they believe should be accepted with some reserve, as even an otherwise good quality of clean root will at times exceed this amount. Umney (*Pharm. J., Lond.*, 1903, p. 879) reports finding from 7.5 to 15.0 per cent of ash, and does not believe it to be practical to establish definite limitations. Of 10 samples reported on in the annual report by Philip Roeder, one yielded 6.58 per cent of ash, while another yielded as high as 17.48 per cent. The contained water varied from 6.31 to 8.53 per cent, and the aqueous extract varied from 23.9 to 41.70 per cent. The water-free drug yielded from 7.19 to 18.72 per cent of ash, and from 26.13 to 45.08 per cent of aqueous extract.—*Pharm. Post, Wien*, 1905, v. 38, p. 391.

Caeser and Loretz recommend the colorimetric estimation of rhubarb according to Tschirch.—*Abstr. in Pharm. Ztg.*, 1905, v. 50, p. 772.

Arzberger (*Pharm. Post*, 1905, No. 12) outlines a method for the detection of turmeric in rhubarb.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 628.

Gadd, H. Wippell and Sydney C., assert that for rhubarb there is no simpler test than that of W. L. Howie (*Pharm. J., Lond.*, 1873), a summary of which is reproduced in *Pharm. J., Lond.*, 1905, v. 21, p. 520.

Caldwell, Paul, asserts that in making the mixture of rhubarb and soda a clear preparation may be obtained by macerating the fluid extracts in the glycerin and spirit of peppermint for two weeks, then adding the water in which the sodium bicarbonate has been dissolved.—*Drug. Circ. & Chem. Gaz., N. Y.*, 1905, v. 49, p. 306.

An abstract points out that recent experiments by Greenish appear to cast doubt on the advisability of using water as a menstruum for rhubarb. He points out that alcoholic liquids are better solvents for the anthraglucosides, and that all heat should be avoided.—*Pharm. Prax.*, 1905, v. 4, p. 18.

The committee on adulteration examined 32 samples of syrup of rhubarb; 14 of these samples contained no potassium carbonate, 4 had insufficient fluid extract of rhubarb, while the remaining 18 appeared to comply with the official requirements.—*Proc. Louisiana Pharm. Ass.*, 1905, p. 43.

Williams, John K., complains that aromatic tincture of rhubarb makes an unsightly preparation when mixed with syrup, and suggests a modification in the method of preparing.—*Proc. Connecticut Pharm. Ass.*, 1905, p. 48.

RHUS GLABRA.

Eberle, E. G., mentions *Rhus glabra* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

RUBUS.

Eberle, E. G., mentions *Rubus villosus* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

SABAL.

Eberle, E. G., mentions *Serenoa serrulata* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Van Zandt, I. L., discusses some of the uses of saw palmetto (Med. Rec., N. Y., 1905, v. 67, p. 937).—Reference from Ind. Med., 1905, p. 675.

Cowperthwaite, A. C., points out that saw palmetto is useful in prostatic troubles, and often in ovarian enlargement. It will aid in the development of undeveloped mammary glands.—Tr. Am. Inst. Homœop., 1905, v. 51, p. 363.

SABINA.

Freeman, William G., makes a comparison of the savin leaves in commerce, and presents some reference to the literature on this drug.—Pharm. J., Lond., 1905, v. 21, p. 829.

Umney and Bennett present a study of a false savin (*Juniperus phoenicia*) and the oil obtained from it.—*Ibid.*, p. 827.

SACCHARUM.

Eberle, E. G., mentions *Saccharum officinarum* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Harlay, M. (*J. de Pharm. et de Chim.*, 1905, v. 21, pp. 49–55), points out that a number of official roots contain cane sugar, and that in the roots of the Umbelliferae the quantity is considerable. The amount of reducing sugar is small, except where the vegetative functions are resumed, or in the case of old or dried organs.—*J. Soc. Chem. Ind.*, Lond., 1905, v. 24, p. 143.

Bollinger, George, asserts that it is difficult to obtain granulated sugar suitable for pharmaceutical manufacturing. He believes that rock candy alone yields a universally satisfactory product.—Pharm. Era., N. Y., 1905, v. 34, p. 580.

Trillat, A., discusses the antiseptic properties of the fumes of sugar, and presents a compilation of his results on colon bacillus, bacillus typhosus, and staphylococcus.—Compt. rend. Acad. d. sc., Paris, 1905, v. 141, pp. 215–217.

Just's Botanischer Jahresbericht (1905, v. 33, part 3, pp. 815-818) contains a number of references bearing largely on the cultivation of the several plants yielding saccharose, the sugar industry as developed in various parts of the world, and the possible utilization of the waste products.

SACCHARUM LACTIS.

An abstract from a Danish patent specification outlines an economic method of producing sugar of milk. The whey is evaporated with the addition of some albuminoid material and the removal of the fat. The resulting syrup is diluted with water and treated with animal charcoal, acetic acid, and magnesium sulphate. After boiling for some time a small portion of alum is added, the liquid is then filtered, and finally evaporated and the sugar allowed to crystallize out.—Chem. Ztg. Cöthen., 1905, v. 29, p. 1286.

The committee on adulteration report finding one sample that contained cane sugar.—Proc. Michigan Pharm. Ass., 1905, p. 79.

An abstract from the annual report of Philip Roeder, Wien, asserts that of 7 samples examined 3 were returned, because of their color, mechanically admixed impurities, or incomplete solubility.—Pharm. Post, Wien, 1905, v. 38, p. 391.

Wetterstroem, Theo. D., examined 4 samples of sugar of milk and found them to vary from 96 to 99.5 per cent of lactose.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 186.

Dekker, J., reviews the several methods proposed for the detection of sugar in sugar of milk.—Pharm. Weekbl., 1905, v. 42, pp. 186-188.

Wöhlk, A., outlines a new color reaction for milk sugar and maltose.—J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 47 (from Ztschr. f. anal. Chem., v. 43).

SALVIA.

Eberle, E. G., mentions *Salvia officinalis* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

SANGUINARIA.

Vanderkleed, Charles E., reports 4 assays of sanguinaria which varied from 2.5 to 4.12 per cent of alkaloids, indicating that the general quality of this drug is very good.—Proc. Penna. Pharm. Ass., 1905, p. 55.

Lloyd, John Uri, points out that sanguinaria is both a contamination and an adulterant of hydrastis. Sanguinaria itself is liable to contamination with other similar fibrous drugs.—Pharm. Rev., 1905, v. 23, p. 332.

Greene, E. L., makes some suggestions regarding *Sanguinaria* and describes 4 new species.—Bull. Torrey Bot. Club., 1905, v. 32, p. 510.

SANTONINUM.

Wedekind and Koch discuss the action of various reagents on santonin and point out that santonin, and such of its derivatives as contain the carbonyl group intact, behave as oxonium compounds with certain metallic haloids. They also discuss the behavior of the halogens with santonin.—Ber. d. deutsch. Chem. Gesellsch, 1905, v. 38, pp. 421-435.

Wedekind, Edgar, discusses the introduction of nitrogen into the santonin molecule, and the physiological behavior of certain santonin derivatives. Of the several compounds that have been studied from a physiological point of view none has any appreciable toxic affect on lower animals, and only santonin itself appears to be capable of destroying ascarides.—J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 134 (from Ztschr. f. Physiol. Chem., v. 43, pp. 240-248).

SAPO.

An abstract (from Pharm. Weekbl.) discusses the preparation of soap and gives formulas for the making of neutral soaps; another article discusses "Savon dentifrice" and gives formulas.—J. de Pharm. d'Anvers, 1905, v. 61, pp. 57-63 and 63-64.

Kippenberger (Zeitschr. f. angew. Chem., 1905) describes and figures an apparatus that is designed to facilitate the uniform heating of the mixture of fat, alkali, alcohol, and water in determining the saponification number of fats and oils.—Pharm. Ztg., Berlin, 1905, v. 50, p. 693.

SAPO MOLLIS.

Caldwell, Paul, unhesitatingly condemns the official formula directing the use of linseed oil, and prefers a soft soap made from cotton seed oil.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 306.

Jacobson recommends making the spiritus saponatus of the Ph. Germ., IV, directly from the olive oil and stick potash, and gives a formula.—Pharm. Ztg., Berlin, 1905, v. 50, p. 792.

SARSAPARILLA.

Fleury, E., discusses the sarsaparillas of to-day, including the roots from Mexico, Honduras, Jamaica, and Para.—Bull. des Sc. Pharmacol., Paris, 1905, v. 12, pp. 190-200.

Philip Roeder reports that a sample of Vera Cruz sarsaparilla root without further preparation contained 10.5 per cent of water and yielded 4.82 per cent of ash, or 5.38 per cent of ash for the water-free drug.—Pharm. Post, Wien, 1905, v. 38, p. 391.

SASSAFRAS.

Eberle, E. G., mentions *Sassafras sassafras* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

SCAMMONIUM.

Guiges, P., points out that scammony is not a true gum resin, but is obtained by manipulating the root with alcohol. It is generally thought that the characteristics of scammony are different from what they were formerly, because of the difference in the origin of the drug from which it is made. It is also thought that the introduction of spurious roots, roots of species of *Jalapa*, is responsible for some of the change. Thus it is known that the root of *Jalapa fusiformis* (*Ipomœa orizabensis* Led.) and the so-called Tampico jalap (*Ipomœa simulans* Hanb.) are widely used as substitutes for scammony.—Pharm. Prax, 1905, v. 4, p. 462 (from J. de Pharm. et de Chim.).

Requier, M. Paul, reports a series of experiments with dried and fresh roots of scammony to determine the amount of saccharose present. He determined the reducible sugar, calculated as dextrose, the saccharose, methyl pentose, and pentose.—J. de Pharm. et de Chim., 1905, v. 22, pp. 435, 487, and 540.

SCILLA.

Lyons, A. B., points out that while the extraction in making the official fluid extract of squill is not complete, it yields a product that is tolerably uniform, provided it is made from a drug of standard strength.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 262.

Nixon, C. F., asserts that the fluid extract of squill is not satisfactory, as the menstruum dissolves the larger amount of mucilage that is contained in the drug.—Apothecary Boston, 1905, v. 17, p. 774.

Gadd, H. Wippell and Sydney C., suggest a dry extract standard for the official Ph. Brit., vinegar of squill.—Pharm. J., Lond., 1905, v. 21, p. 520.

SCOPOLA.

Maben, Thomas, points out that the only new alkaloidal drug introduced in the U. S. P., VIII, is scopola, the standard for which is 0.5 per cent of "its alkaloids," which are spoken of in the description of the extract and the fluid extract as "mydriatic alkaloids," but thinks the variation is unintentional.—Pharm. J., Lond., 1905, v. 21, p. 141.

Williams, S. W., believes that the admission of scopola "is a well warranted recognition of a good thing"—"It stands a practical equivalent of belladonna."—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 308.

SCOPOLAMINÆ HYDROBROMIDUM.

Lyons, A. B., points out that the name of the species from which the alkaloid is obtained should have been given, and the "other plants" should have been specified, or at least the expression changed

to "some other plants." The identity of scopolamine with hyoscine is affirmed without sufficient warrant. Isomers are not now considered chemically identical. The revision committee was not called upon to settle the disputed question whether scopolamine and hyoscine are therapeutically identical. It is a fact that manufacturers have assumed this, and that when physicians prescribe hyoscine they almost invariably get scopolamine. It was to justify this substitution that scopolamine was made official, but the pharmacopœia should not have committed itself to an opinion on a scientific question as yet undecided.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 262.

Siedler, P., asserts that the melting point of this substance is given in the Ph. Germ., IV, as 180° C. He found that material that was dehydrated over sulphuric acid and then dried for two hours at 100° C. softens at 187° C. and melts at from 191° to 192° C. It is quite necessary to remove even traces of water, otherwise this substance will melt at abnormally low temperatures, even so low as 100° C. Material that has been melted at low temperatures will require from 191° to 192° C. to remelt it after it has once cooled.—Pharm. Post, Wien, 1905, v. 38, p. 568.

Kobert, R., points out that the melting point of scopolamine is reduced slightly by the addition of a small amount of the inactive scopolamine, but is again increased by the addition of a larger amount of the same substance. For these reasons he believes that the melting point determination, *per se*, is not sufficient guarantee of the purity or the identity of the alkaloid to be used for therapeutic purposes.—Riedel's Berichte, 1905, p. 22.

Schmidt, Ernst, presents a comprehensive study of the behavior of scopolamine and scopoline with a number of reagents.—Arch. d. Pharm., 1905, v. 243, p. 559.

Kobert, R., discusses the wide field of usefulness of scopolamine, the untoward effects of some of the accompanying substances, and points out the necessity for insuring the absence of all optically inactive substances. He also presents a number of references to the literature relating to scopolamine and its uses.—Riedel's Berichte, 1905, pp. 9–22.

Whitacre, Horace J., discusses the dangers from scopolamine-morphine anæsthesia and concludes (1) that scopolamine-morphine anæsthesia is not devoid of danger; (2) that the use of scopolamine-morphine alone for surgical narcosis is not justifiable; (3) that a single dose two hours before operation lessens the discomforts attendant on the operative procedure to a high degree, and may obtain a definite place in surgical practice. The author also records several deaths that have occurred from the use of this anæsthetic.—J. Am. M. Ass., 1905, v. 45, p. 2026.

DeMaurans (Sem. Méd., Paris, v. 25) cites a total of 22 deaths occurring from the use of scopolamine-morphine. He concludes that "anyone using this notoriously unreliable and dangerous technique incurs a heavy responsibility."—J. Am. M. Ass., 1905, v. 45, p. 1991.

A number of additional references on the use of scopolamine-morphine as an adjunct to other anæsthetics and also as a means for producing more or less profound anæsthesia will be found in the Journal of the American Medical Association and in the Index Medicus.

SCUTELLARIA.

Eberle, E. G., mentions *Scutellaria laterifolia* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Lloyd, John Uri, points out that the typical species (*S. laterifolia*) should be used in medicine: unfortunately the *S. versicolor* and *S. canescens*, larger and more robust, are generally collected. Consequently the purchaser of "scull cap" needs to exercise exceeding care if he would secure the species which should be used.—Pharm. Rev., 1905, v. 23, p. 332.

SENEGA.

Eberle, E. G., asserts that several of the Polygalas of Texas have the properties of the official.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 306.

Hood, C. S., in an article on "Botany and its relations to the pharmacist," discusses the introduction of senega root into medicine, its origin, and the source of the root at the present time.—Western Druggist, 1905, v. 27, p. 773.

The Bureau of Plant Industry reports having senega under observation, though as yet they have not succeeded well with its cultivation.—Ann. Rep. Dept. Agric., 1905, p. 148.

Caeser and Loretz point out that the price of senega is advancing steadily, while the quality is decreasing. For estimating the value of the drug, color, thickness, and freedom from dirt are of importance, light-colored, comparatively thin roots being preferred.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 621.

In the laboratory of Philip Roeder, Wien, a sample of powdered senega was found to contain 8.04 per cent of water, 3.37 per cent of ash, and to yield 27.11 per cent of water soluble extract.—Pharm. Post, Wien, 1905, v. 38, p. 391.

The revisors of Vienna pharmacies found senega which yielded as high as 15.96 per cent of ash, and point out that in the more recent literature an ash content of from 2.5 to 3.22 per cent is recorded as being normal.—Pharm. Prax., 1905, v. 4, p. 38.

Schröder, A. (Arch. d. Pharm.), examined the fatty oil present in the dry root of senega to the extent of about 0.5 per cent. He

describes it as being a thick, dark-brown liquid, having a mild, but rather rancid, odor. It is freely soluble in ether, chloroform, benzole, acetone, and carbon disulphide, though less readily soluble in alcohol, xylol, and petroleum ether, the latter leaving a portion of the oil undissolved. The specific gravity of the oil was 0.9616 at 18° C. The saponification number 193.52–194.14. The iodine number with the unsaponifiable matter \$1.65 to \$2.05, and without the unsaponifiable fat 75.13 to 75.61. The latter amounted to 17.78 per cent of the total oil.—Pharm. Ztg., 1905, v. 50, p. 1031.

SENNA.

True, Rodney H., points out that both Tinneville and Alexandria senna do well in this country. The season at Washington is too short, but an excellent growth of the plant and a good crop of leaves have been secured at the Texas station. The plants are hardy there and live as escapes.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 275.

Moore, Russell W., asserts that senna is generally of good quality, 6 samples showing an average of 37.06 per cent of soluble matter, and in every case well above the standard of 28 per cent.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 266.

Moore, Russell W., finds that the determination of soluble matter is best made by boiling 10 gm. of the sample with water in a liter flask, evaporating an aliquot part of the resulting solution, previously filtered, and weighing. The Treasury regulations require 28 per cent of soluble matter.—J. Am. Chem. Soc., 1905, v. 27, p. 614 (from J. Soc. Chem. Ind., 1905, v. 24, p. 487).

Vanderkleed, Charles E., outlines a method for the assay of emodin-yielding drugs.—Proc. Pennsylvania Pharm. Ass., 1905, p. 193.

The revisors of Vienna pharmacies report finding argol leaves as an adulterant of senna. These leaves had become comparatively scarce.—Pharm. Prax., 1905, v. 4, p. 38.

SERPENTARIA.

True, Rodney H., points out that serpentaria is grown regularly in the testing gardens of the Bureau of Plant Industry.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 275.

Hood, C. S., discusses some of the problems that arise in connection with the cultivation of serpentaria, owing to its extremely slow growth.—Western Druggist, 1905, v. 27, p. 775.

SERUM ANTIDIPHThERICUM.

Rosenau, M. J., describes the methods by which the immunity unit for measuring the strength of diphtheria antitoxin is obtained and the principles involved. This unit is based on Ehrlich's normal

serum and is the official standard prepared under the act approved July 1, 1902. He also presents a comprehensive bibliography of the literature bearing on the standardization of diphtheria antitoxin.—Bull. No. 21 Hyg. Lab., U. S. P. H. & M.-H. S., 1905 (April), 92 pp.

The Spanish Pharmacopœia includes this article under the title "Suero Antidiftérico," the Latin title being "Serum Antidiphthericum." It is defined as being serum obtained from the blood of animals (preferably the horse) of guaranteed health and immunized artificially against diphtheria. The liquid serum and the dried are defined and the method for its employment is outlined.—Farmacopea Oficial Española, 1905, pp. 539-540.

Layson, L. C. (American Medicine, 1905, October 28), reports a laboratory study of antidiphtheritic serum. He concludes that serums retain their activity much longer than has heretofore been supposed, being unimpaired or but slightly modified at the end of two, four, or even five years.—J. Am. M. Ass., 1905, v. 45, p. 1520.

"The New Idea" discusses the production of antitoxin sera, the tests that are made in connection with the production of antidiphtheritic serum, and criticises the immunizing dose prescribed in the U. S. P., VIII.—The New Idea, 1905, v. 27, pp. 41-47, 64-65, 136, and 145.

McCollom (Bost. M. & S. J., 1905) records the experience of nine years in the treatment of diphtheria with antitoxin.—Therap. Gaz., 1905, v. 29, p. 620.

Wainwright, J. W., discusses the general subject of serum therapy. (International Clinics, 1905, v. 3.) J. Am. M. Ass., 1905, v. 45, p. 1608.

Street, St. C. (Med. Rec., 1905, November 12), reports a case in which 67,000 units of antitoxin were administered before there was any response to treatment. *Ibid.*, p. 1758.

SINAPIS.

Eberle, E. G., mentions *Sinapis alba* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Kebler, Lyman F., reports powdered mustard adulterated with turmeric colored wheat starch.—*Ibid.*, p. 186.

Tschirch and Oliva present a comprehensive study of the several seeds of the crucifera, with particular reference to the variations found in the seed coat of the several species of mustard.—Schweiz. Wchnschr. f. Chem. u. Pharm., 1905, v. 43, p. 614.

Spaeth, E., points out the difficulty of detecting powdered rape seed meal in powdered mustard. He enumerates among the more common adulterants of powdered mustard, wheat flour, corn meal,

and the addition of coal tar dyes. Commercial mustard should contain not more than 4.5 per cent of ash and not more than 0.5 per cent insoluble in 10 per cent hydrochloric acid.—Ztschr. f. Unters. d. Nahr. u. Genussm., 1905, v. 10, p. 32.

Leach, A. E., discusses the determination of added mustard hulls in ground mustard and suggests the following limits for ground mustard, expressed on the dry, fat free substance:

The reducing matter (as dextrose) should not exceed 2.5 per cent, the crude fibre should not exceed 5 per cent, and the total nitrogen should be not less than 8 per cent. As shown by the microscope the sample should be free from more than minute traces of starch and should not exhibit an excess of hulls over seed tissue.—Analyst, Lond., 1905, v. 30, p. 59.

Hartwich and Vuillemin have examined 36 samples of mustard and present an exhaustive record of their findings.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 394.

Vuillemin (Pharm. Zentralh., 1905, v. 45, p. 384) proposes a modification of Dietrich's method for determining the amount of mustard oil, the final product being silver sulphide.—Analyst, Lond., 1905, v. 30, p. 59.

Schimmel & Co. discuss the work done by Hartwich and Vuillemin on the determination of mustard oil in seed.—Semi-Ann. Rep. Schimmel & Co., 1905, Oct.-Nov., p. 49.

Barford (Svensk. Farm. Tidskr.) elaborates on the work done by J. W. Hammer in connection with the volatile oil content of mustard seed. The greater number of the samples of mustard seed examined contained more volatile oil than is required by the Ph. Ger., IV.—Pharm. Ztg., Berlin, 1905, v. 50, p. 563. See also Arch. f. Pharm. og Chem. Copenhagen, 1905, v. 12, pp. 34-37.

Salvert, A., outlines a method for the estimation of sulphur compounds in mustard.—Bull. Soc. de pharm. de Bordeaux, 1905, v. 45, pp. 142-146.

Süss, P., (Pharm. Zentralh., v. 46, p. 291) discusses the artificial coloring of mustard and methods for detecting the same.—Pharm. J., Lond., 1905, v. 21, p. 33.

SODII ACETAS.

Bauer, C., describes the manufacture of sodium acetate from pyroligneous acid.—J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 275 (from Chem. Ztg., 1905, v. 29, p. 181).

SODII ARSENAS.

Wulff, C., presents a comparative study of the requirements for sodium arsenate as recorded in the several pharmacopœias.—Apoth. Ztg., Berlin, 1905, v. 20, p. 1029.

SODII BICARBONAS.

Havenhill, L. D., reports that of 10 samples of sodium bicarbonate examined only 4 gave clear solutions in water and conformed strictly to U. S. P. requirements. Four of the remaining samples contained an excess of normal carbonates.—*Proc. Kansas Pharm. Ass.*, 1905, p. 92.

Weathers, L. C., has examined 75 samples of sodium bicarbonate, the majority of which he found to be only fair. He points out that the amount of acid required to neutralize them was almost invariably high and concludes that all samples contain some normal carbonate.—*Proc. Massachusetts Pharm. Ass.*, 1905, p. 101.

Casamada (Rép. de Pharm.) outlines a simple method for the estimation of sodium bicarbonate, based on the behavior of the bicarbonates and the carbonates to the different indicators. He titrates with normal HCl, using first phenolphthalein and then methyl orange as indicators.—*Pharm. Ztg.*, Berlin, 1905, v. 50, p. 751.

Luckey, Benj., recommends the use of sodium bicarbonate as a mouth wash: one teaspoonful in an ordinary glass of tepid water, three or four times a day.—*Dental Cosmos*, Phila., 1905, v. 47, p. 522.

SODII BORAS.

Lloyd, John Uri, points out that, owing to competition in prices, trade borax is found to vary in composition from sodium bicarbonate, nearly pure, to borax mixed with only a moderate amount of sodium bicarbonate. Seemingly the amount of the admixture depends upon the price the drug commands, and the efficiency of the officials and the adulteration laws of the locality in which the preparation is sold.—*Pharm. Review*, 1905, v. 23, p. 299.

SODII BROMIDUM.

Caspari, Charles E., reports on 18 samples of sodium bromide, 10 of which satisfied the official requirements, 4 contained an excess of sodium chloride, one contained metallic impurities, and 3 contained dirt.—*Proc. Missouri Pharm. Ass.*, 1905, p. 75.

SODII CARBONAS.

Lyons, A. B., points out that there is an inconsistency between the statements of the solubility of sodium carbonate monohydrated and that of the sodium carbonate at the former pharmacopœia.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 260.

Hensel, Samuel T., discusses the production of sodium carbonate, the several processes in use at the present time, and includes an

account of the natural sodium carbonate found in Mexico.—The *Spatula*, 1905, v. 11, pp. 327–328 and 398–401.

Kebler, Lyman F., asserts that sodium carbonate is one of the most difficult agents to procure of the required purity, as a chemical reagent. It is usually contaminated more or less with chlorides.—*Proc. Off. Agric. Chem.*, 22 Ann. Conv., p. 187.

SODII CITRAS.

Patch, Edgar L., reports two samples of sodium citrate insoluble in 20 parts of water. One contained an excess of lead.—*Proc. Am. Pharm. Ass.* 1905, v. 53, p. 189.

SODII IODIDUM.

Caspari, Charles E., says that of four samples of sodium iodide examined not one answered the official requirements. Three samples contained an excess of alkali, three contained iodate, one contained potassium, and one contained metallic impurities.—*Proc. Missouri Pharm. Ass.*, 1905, p. 75.

SODII NITRAS.

Tschernobajeff, D., recommends that chlorates and perchlorates be determined together by Lemaitre's method of reduction with sodium sulphite, and the chlorates be determined separately by reduction in the cold by means of iron and sulphuric acid according to Hendrixson's method.—*Expt. Sta. Rec.*, v. 17, p. 7 (from *Chem. Ztg.*, 1905, v. 29, pp. 442–443).

SODII PHOSPHAS.

Kebler, Lyman F., reports finding appreciable quantities of arsenic in sodium phosphate. Five of the samples examined contained from 30 to 52 milligrammes of arsenic in 100 grammes.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 189.

Hoffmann, Aug., points out that the *Ph. Germ.*, IV, test for the presence of sulphuric acid in sodium phosphate is liable to be misleading because of the failure to prescribe the quantities of nitric acid and of barium nitrate to be employed, and the relations of these to each other and to the solution of the salt.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 714.

Thornton, E. Q., says that "*Liquor Sodii Phosphatis Compositus*" of the *U. S. P.*, VIII, has little to recommend it. The reputation of sodium phosphate as a hepatic stimulant was established from the use of the salt, and not from a solution like this.—*Therap. Gaz.*, 1905, v. 29, p. 737.

SODII SALICYLAS.

Caspari, Charles E., asserts that of 19 samples of sodium salicylate examined, not one reached the standard set by the pharmacopœia. Fifteen samples contained more or less chloride, 7 contained sulphate, 9 samples yielded turbid aqueous solutions, 2 contained metallic impurities causing the samples to have a dirty appearance, and 7 contained more or less carbonizable material.—Proc. Missouri Pharm. Ass., 1905, p. 76.

The committee on adulteration reports that of many samples examined not one conformed strictly to the requirements of the U. S. P. Most of the samples contained chlorides, some contained sulphates, and one contained a metallic impurity. Only a few of the samples gave a clear solution in water.—Proc. Michigan Pharm. Ass., 1905, p. 79.

SPARTEINÆ SULPHAS.

Moureu and Valeur report on an exhaustive study of iodomethylates and other iodine compounds of sparteine; also an attempt to demonstrate the probable constitution of this alkaloid.—J. de Pharm. et de Chim., 1905, v. 22, pp. 481, 485, 529, and 531. Also Compt. rend. Acad. d. sc. Par., 1905, v. 141, pp. 49-51, 117-119, 261-262, and 328-330.

Reichard (Pharm. Zentrallh.) records a number of tests for sparteine, coniine, and nicotine.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 291.

Willstätter and Marx controvert the suggestion made by Ahrens, that sparteine is a double combination: they suggest the use of chromic acid as a desirable oxidizing agent.—Ber. d. deutsch. chem. Gesellsch., 1905, v. 38, pp. 1772-1780.

SPIGELIA.

Eberle, E. G., mentions *Spigelia marilandica* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Rusby, H. H., points out that because two or three plants are called "pinkroot" in our Southern States our official spigelia is spurious or adulterated, probably to the extent of 75 per cent of all sold, and the adulterant is entirely worthless.—Merck's Rep., N. Y., 1905, v. 7, p. 212.

The Bureau of Plant Industry reports a careful study of the crude drug known as pinkroot, and finds that much confusion exists concerning the true and efficient drug.—Ann. Rep. Dept. Agric., 1905, p. 149.

Stockberger, W. W., presents historical data in reference to pinkroot (*Spigelia marilandica*), referring particularly to the early con-

fusion between this drug and *Spigelia anthelmia* of the West Indies. He also discusses at some length the later confusion of *Ruellia* for *Spigelia*, which still persists in some recent text-books, and points out that the latter drug is relatively inert.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 324-326.

SPIRITUS ÆTHERIS COMPOSITUS.

Caldwell, Paul, asserts that manufacturers frequently omit the oil of wine in this preparation.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 306.

SPIRITUS ÆTHERIS NITROSI.

Furbush, Willis St. L., has experimented with a number of processes proposed for the production of spirit of nitrous ether, and concludes that U. S. P., 1890, method is the most readily followed. He has also examined a number of samples of commercial spirit of nitrous ether, practically all of which were deficient in some respects, and suggests that the pharmacist should make his own spirit of nitrous ether.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 587 (from J. Alumni Ass., Mass. Col. Pharm., 1905, p. 6-14).

LaWall, Charles H., reports samples of spirit of nitrous ether which varied from 0.15 to 2.40 per cent of ethyl nitrite.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 186.

Patch, Edgar L., examined 20 samples of spirit of nitrous ether, the average ethyl nitrite content was 2.78 per cent, one sample was below 1, and one sample above 4 per cent.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 189.

SPIRITUS AMMONIÆ AROMATICUS.

Fiske, Frank E., discusses the variable character of aromatic spirit of ammonia, as usually found in the shops, points out some of the causes for this variability, and outlines a process which he believes would be more readily followed.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 393.

SPIRITUS FRUMENTI.

An editorial note discusses the precautions that were taken by the Scottish Parliament centuries ago to define the nature of whisky, and to protect the purity of the Scotch product. The article reproduces a number of excerpts, relating to the use and production of whisky, from old documents.—Lancet, Lond., 1905, v. 1, p. 240.

Schidrowitz and Kaye present a communication on the chemistry of whisky, in the course of which they tabulate their results with Highland malts, Lowland malts, Cambeltowns, Islays, and grain whiskies.—J. Soc. Chem. Ind., Lond., 1905, v. 24, pp. 585-589.

Walker and Schreiber have made a comparative study of a number of methods proposed for the detection of artificial coloring matter in whisky. The authors finally recommend (1) removing the color by chloroform, (2) determining the color insoluble in water, (3) determining the color insoluble in water and extracted by ether, and (4) an amyl alcohol test. In addition, they recommend noting the character of the solid matter, applying an iron alum test, and a lead subacetate test.—*Proc. Ass. Off. Agric. Chem.*, 22 Ann. Conv., pp. 60–62.

Crampton, C. A., reports a comparative study by a number of analysts of four samples of whisky or distilled liquor. The results obtained by the several analysts are given in a table. Some additional comments by the several referees are also included.—*Ibid.*, pp. 45–60.

SPIRITUS GLYCERILIS NITRATIS.

Wilbert, M. I., questions the advisability of changing the name of this spirit, the word “glonoin” having become well established.—*Am. J. Pharm., Phila.*, 1905, v. 77, p. 360.

Binz, C., discusses the therapeutic application of glyceryl trinitrate, reviews the literature regarding its use, and reports a study of the decomposition of the compound, with some suggestions on the more desirable method of using or of prescribing it. The word “glonoin” is given as being derived from the initial letters of the constituents: glycerin, oxygen, nitrogen, and oxide, with the terminal ending in.—*Therap. d. Gegenw.*, Berlin, 1905, v. 46, pp. 49–55.

An editorial discusses the “value of nitroglycerin,” and a second, “tolerance to nitroglycerin,” and asserts that when

Given in well-made gelatin-coated pills or compressed tablets, the pill or tablet is so slowly absorbed that the physiological influence persists over a considerable period of time.—*Therap. Gaz.*, 1905, v. 29, pp. 382–383 and 525–526.

Loomis, H. P., discusses the limitations of the value of nitroglycerin as a therapeutic agent.—*Med. Rec., N. Y.*, 1905, v. 67, pp. 411–413; reference from *Ind. Med.*, 1905, p. 355.

SPIRITUS VINI GALLICI.

Hehner, Otto, discusses the proper application of the word brandy, and reviews the literature pertaining thereto.—*Analyst, Lond.*, 1905, v. 30, pp. 36–56.

Jackson, Geo. H., presents a detailed description of the methods employed in the manufacture of Cognac brandy, and defines the terms used in the industry. He also discusses the changes in composition due to ageing, etc.—*J. Am. Chem. Soc.*, v. 27, 1905, p. 522 (from *Daily Consular Rep.*).

Fairley, T., discusses the history of distilled spirit, especially brandy and whisky, and gives some additional information, with illustrations, regarding the methods of preparing the several kinds of distilled liquors that are used in various parts of the world.—*Analyst*, Lond., 1905, v. 30, pp. 293–306.

Rocques, M. X., reports experiments in the analysis of brandy that are designed to demonstrate the need for the adoption of uniform methods of procedure.—*Ann. de Chim. analyt.*, 1905, pp. 63–65.

STAPHISAGRIA.

Moore, John Murray, suggests the use of staphisagria in seminal weakness.—*Hahneman. Month.*, Philada., 1905, v. 40, p. 637.

STILLINGIA.

Eberle, E. G., mentions *Stillingia sylvatica* among the medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 305.

STRAMONIUM.

Eberle, E. G., includes *Datura stramonium* among the medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 305.

True, Rodney H., says that stramonium has been successfully grown in the testing gardens at Washington.—*Ibid.*, p. 274.

The Bureau of Plant Industry reports that at Ebenezer, S. C., experiments in the cultivation of stramonium are being conducted on rather a large scale. Several hundred pounds of the leaf were grown, cured by artificial heat in a tobacco barn, and marketed at a price in advance of the highest quoted figure.—*Ann. Rep. Dept. Agric.*, 1905, p. 148.

Vanderkleed, Charles E., reports two assays of stramonium which yielded 0.310 and 0.350 per cent of alkaloid, respectively.—*Proc. Pennsylvania Pharm. Ass.*, 1905, p. 57.

Feldhaus, J., has made an exhaustive examination of the several parts of stramonium and records the amount of alkaloid found in each.—*Arch. d. Pharm.*, 1905, v. 243, p. 328.

Naylor, W. A. H., points out that, as the mixed alkaloids in stramonium are understood to be the same as those contained in belladonna, there seems to be no good reason why a process should not be given in the *Ph. Brit.* for the assay of these preparations. The mixed alkaloids might with advantage be subjected to reexamination as complete as has taken place in the case of henbane.—*Pharm. J.*, Lond., 1905, v. 21, p. 127.

An abstract (from *Bull. Imp. Inst.*, *Suppl. Brd. Trade J.*, 1905) points out that a sample of the seed of *Datura stramonium* from Bushar, India, contained 0.26 per cent of hyoscyamine, as compared

with 0.35 per cent of the same alkaloid found in Egyptian and European specimens. No other alkaloids present in any of these specimens.—J. Soc. Chem. Ind., Lond., 1905, v. 24, p. 149.

An abstract from Helfenberger Annalen points out that stramonium leaves corresponding to all of the requirements of the Ph. Germ., IV, gave the following amounts of extract when exhausted with: Alcohol (90 per cent), 8.88–9.13 per cent; alcohol and ammonia, 9.55–9.62 per cent; water, cold, 29.68–30.06 per cent; water, hot, 28.40–29.04 per cent.—Pharm. Ztg., Berlin, 1905, v. 50, p. 672.

STRONTIUM.

Richards, Theodor William, discusses the atomic weight of strontium and records experiments made to determine the correct weight, which the author concludes should be given as 87.662 (translated from the Proc. Am. Acad., v. 40, 1905).—Ztschr. f. anorgan. Chem., 1905, v. 47, pp. 146–147.

STROPHANTHUS.

Gilg, Ernst, discusses the pharmacognosy of strophanthus and the literature of this drug. He devotes particular attention to the consideration of *Strophanthus gratus*, which he illustrates.—Arb. a. d. Pharm. Inst. d. Univer., Berlin, 1905, v. 2, pp. 59–72.

An editorial (in Pharm. Ztg., 1905, p. 178) asserts that the seeds of *Strophanthus gratus* are less liable to be mistaken or substituted than are those of *S. kombé*, and are characterized by uniform and reliable activity.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 600.

Rusby, H. H., points out that no drug is more certain or prompt in its action, or used in more urgently vital cases than strophanthus, yet more than 75 per cent of that used is probably spurious. One spurious variety is nearly inert and another appears to exert a toxic action out of proportion to its therapeutic effect.—Merck's Rep., N. Y., 1905, v. 14, p. 212.

Dohme, A. R. L., points out that while *Strophanthus kombé* was hailed as being the best variety, figures show that in reality the reverse is true and that *Strophanthus hispidus* is somewhat richer in strophanthin than the *kombé* variety. The laboratory records show a variation from 2.1 per cent of strophanthin in 1901 to 3.0 per cent in 1904 in the *kombé* variety. During the same period *S. hispidus* varied from 2.66 per cent of strophanthin in 1900 to 3.60 per cent in 1904.—Apothecary Boston, 1905, v. 17, p. 942.

Thoms, H., discusses the chemistry of strophanthus and reviews the literature relating thereto. Also discusses the several strophanthins that have been isolated and includes a proposed description for g-Strophanthinum crystallisatum.—Arb. a. d. Pharm. Inst. d. Univer., Berlin, 1905, v. 2, pp. 74–87.

Caeser and Loretz discuss the variability of the available strophanthus seeds. This variability they believe to be due to the lack of care in selecting the available supplies, and point out that the physiological test is the only satisfactory means for differentiating the several seeds. They also outline a method for the determination of strophanthin which provides for the extraction of the crushed seeds with 70 per cent alcohol, in connection with a reflux condenser. The alcohol is evaporated by means of a water bath and the fat removed from the residue by means of benzin. The resulting extract is dissolved in boiling water and the extractive precipitated with lead acetate solution. The lead salt is removed by means of hydrogen sulphide and heat, and the solution filtered and finally evaporated, in a tared capsule, so as to facilitate the weighing of the resulting strophanthin. The latter may be further purified by a process which they outline.—*Geschäfts-Ber. von Caeser & Loretz, in Halle a. S., 1905, pp. 60 and 100.*

Four samples of strophanthus were examined in the laboratory of Philip Röder, Wien, and found to contain from 30.99 to 35.00 per cent of fatty oil and to yield from 2.43 to 3.55 per cent of strophanthin. The fat-free powder yielded from 3.76 to 5.32 per cent of strophanthin.—*Pharm. Post, Wien, 1905, v. 38, p. 392.*

Naylor, W. A. H., points out that it is essential to have mature seeds from a species which yields uniformly active strophanthin. He refers to the work done by Gilg, Thoms, and Schedel, and their evident preference for the seeds of *Strophanthus gratus*.—*Pharm. J., Lond., 1905, v. 21, p. 127.*

Thornton, E. Q., notes the absence of any reliable chemical assay for strophanthus and asserts that physicians should employ a product that has been physiologically tested.—*Therap. Gaz., 1905, v. 29, p. 739.*

Santesson, G., points out that, in view of the great variability of the tinctures of strophanthus, physiological standardization appears to be desirable.—(*Münch. Med. Wchnschr., 1905.*) *Proc. Am. Pharm. Ass., 1905, v. 53, p. 599.*

Schedel, H., reviews the history and the literature of the pharmacologic and clinical use of strophanthus. The article is illustrated by a number of tracings and includes a comprehensive bibliographic list.—*Arb. a. d. Pharm. Inst. d. Univer., Berlin, 1905, v. 2, pp. 88–99.*

Zilinski, W. (*Wratschebnaja Gazeta, 1905, No. 35*), discusses the action of strophanthin, convallamarin, and caffeine, and points out that strophanthin as well as convallamarin increases the strength of the contractions, while the number of contractions is reduced. The conditions for the nourishment of the heart are therefore more favorable with strophanthin or with convallamarin than they are with caffeine.—*Biochem. Centralbl., 1905, v. 4, p. 495.*

Santesson, C. G. (Scandin. Arch. f. Physiol., Leipz., 1905, v. 17, pp. 389-413), discusses the variability in activity of the seeds and the tincture of strophanthus as found in Swedish pharmacies.—Reference from Ind. Med., 1905, p. 177. See also Svensk. Farm. Tidskr., 1905, v. 9, pp. 261-267 and 286-288.

Carlinfanti, E. (Bolletino Chimico Farmaceutico, v. 43), reports a series of experiments with strophanthus. For the removal of the oil he recommends benzin, and asserts that this does not remove even a trace of active substance from the drug.—Am. Druggist, N. Y., 1905, v. 47, p. 2.

Barbieri, G., disagrees with Carlinfanti in some of his observations on tincture of strophanthus, and the latter replies.—Boll. Chim. Farm., 1905, v. 44, pp. 337-347 and 451-453.

Nine samples of tincture of strophanthus were examined in the laboratory of Philip Röder, Wien, and found to vary from 0.8165 to 0.9029 in specific gravity and to contain from 0.36 to 1.32 per cent of extract.—Pharm. Post, Wien, 1905, v. 38, p. 393.

Caldwell, Paul, asserts that in making the tincture of strophanthus the drug should be washed with purified benzin before it is treated with the menstruum. This he believes would insure a tincture that would not become cloudy.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 307.

STRYCHNINA.

Beckurts, H., presents a study of the action of bromine on strychnine hydrobromide.—Arch. d. Pharm., 1905, v. 243, p. 493.

Reichard (Chem. Ztg., v. 28, p. 977) presents a review of the available tests and reactions of strychnine and brucine, and suggests several modifications.—Pharm. Prax., 1905, v. 4, p. 309.

Pictét and Mattison record a series of experiments with hydrogen peroxide, by means of which they were enabled to produce a series of oxidation compounds of strychnine, which they believe will aid in solving the question of the chemical structure of strychnine.—Ber. d. deutsch chem. Gesellsch., 1905, v. 38, p. 2782.

Bacovescu and Pictét review the work of previous workers, beginning with the work done by Gal and Etard in 1879 (Bul. Soc. chim., v. 31, p. 98), who appear to have been the first to note the action of baryta water on strychnine. The dihydrostrychnine of these early investigators is believed to be identical with strychnol, while the trihydrostrychnine is identical with what Bacovescu and Pictét call isostrychnine. The pharmacologic action of isostrychnine is thought to be more closely related to that of brucine, in fact to be intermediate between brucine and curare.—*Ibid.*, pp. 2787-2792.

Trotman and Hackford discuss the use of strychnine or of a salt of strychnine for the determination of tannin and materials used for

their tannin content.—*J. Soc. Chem. Ind., Lond.*, 1905, v. 24, pp. 1096–1100.

Meier, H., has prepared a strychnine antitoxin by injecting animals (rabbits) with slowly increasing doses of strychnine. The serum of such animals, when injected into other animals, increased their resistance to strychnine quite markedly, the immunity lasting from three to four days.—*Abstr. in Pharm. Ztg.*, 1905, v. 50, p. 804.

Petrow, W. I., reports a number of observations on the destruction of the alkaloids strychnine, caffeine, and atropine in the animal organism, and concludes that strychnine is not materially changed by the several organs examined.—*Biochem. Centralbl.*, 1905, v. 4, p. 495 (from a dissertation, St. Petersburg, 1905).

Igersheimer, J., discusses the action of strychnine on the heart of cold-blooded and warm-blooded animals.—(*Arch. f. exper. Path. u. Pharmakol.*, 1905–6, v. 54, pp. 73–87.) Reference from *Ind. Med.*, 1906, p. 172.

STYRAX.

Ahrens and Hett (*Pharm. Zentrallh.*, v. 45, p. 571) base a test for the purity of storax on the ready solubility of the resinous adulterants in cold petroleum benzin, genuine storax being only very slightly soluble.—*Analyst, Lond.*, 1905, v. 30, p. 60.

The annual report of Philip Röder, Wien, points out that Ahrens gives the acid number of petroleum benzin extract of storax as being between 36.6 and 62.9, and the saponification number as being between 194.6 and 198.4. Thirteen samples of storax were examined and were found to vary in: Acid number from 57.5 to 94.0, saponification number from 180.5 to 200.5, ester number from 86.5 to 134.0. The petroleum benzin extract of eight samples was examined and found to vary for: Acid number from 31.5 to 101.0, saponification number from 180.0 to 202.5, ester number from 80.5 to 162.5. Two of the samples were found to be contaminated with resin and refused.—*Pharm. Post, Wien*, 1905, v. 38, p. 392.

SULPHUR.

Domergue, A. (*J. de Pharm. et de Chim.*, v. 20, pp. 493–499), points out that there should be a distinction between flowers of sulphur and sublimed sulphur. The former name should be reserved for commercial products giving at least 33 per cent of sulphur insoluble in carbon disulphide at the time of manufacture, while the other products of the condensation chamber should be termed sublimed sulphur.—*Analyst, Lond.*, 1905, v. 30, p. 92.

Lyons, A. B., asserts that in the test for arsenic, instead of dissolving the residue in 100 cc. of HCl and then testing by

Gutzeit's test, the residue should be reduced with sulphuric acid and sulphurous acid, as directed on page 522, U. S. P., VIII.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 260.

Ceruti (*Boll. Chim. Farm.*, v. 43, p. 421) outlines a test for sulphur by dissolving in aniline, of the boiling point 180–185, precipitating with acid and weighing.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 1345.

Lunge, G., gives a description of the method developed by Herman Frash to extract sulphur from the deeply covered sulphur beds of Louisiana and an account of the success that has attended these efforts.—*Ztschr. f. angew. Chem.*, 1905, v. 18, pp. 1009–1010.

Bolis, A., points out that the expert engineer sent out by the Italian Government to study the production of sulphur in the United States reports that the sulphur as produced in the State of Louisiana is almost pure (90 to 98 per cent) and that the cost of production is comparatively low.—*Chem. Ztg. Cöthen.*, 1905, v. 29, p. 984.

Hart, Edward, in a review of the problems of industrial chemistry, says that the amount of sulphur taken from the Louisiana deposits is said to average 16,000 tons per month. Upward of 23,000 tons have been taken from a single well. The existence of 40,000,000 tons has been proven.—*J. Am. Chem. Soc.*, 1905, v. 27, p. 158.

Havenhill, L. D., examined 8 samples of precipitated sulphur; 3 contained nonvolatile matter, from 0.21 to 0.42 per cent, while the remaining 5 contained from 37 to 50 per cent of calcium sulphate.—*Proc. Kansas Pharm. Ass.*, 1905, p. 92.

Caspari, Charles E., reports finding one sample of precipitated sulphur containing 52 per cent of calcium sulphate—*Proc. Missouri Pharm. Ass.*, 1905, p. 76.

Ryan, J. J., found 4 samples of precipitated sulphur which contained calcium sulphate varying from 15 to 47.5 per cent; 4 additional samples contained traces of calcium chloride.—*Proc. Massachusetts Pharm. Ass.*, 1905, p. 104.

SUPPOSITORIA.

Wilbert, M. I., discusses the official description of suppositories and notes the failure to provide for the molding of suppositories by cold compression.—*Am. J. Pharm.*, 1905, v. 77, p. 366.

van der Wielen, P., discusses the making of suppositories and related products having oil of theobroma as a base, and the incorporation of water-soluble ingredients.—*Pharm. Weekbl.*, 1905, v. 42, pp. 290–291.

SYRUPUS.

Alcock, F. H., suggests the addition of a trace of potassium carbonate (1 grain to 12 ounces of the finished product) to the *Ph. Brit.*

Syrup to prevent crystallization.—Pharm. J., Lond., 1905, v. 21, p. 750.

Caldwell, Paul, believes that for syrup of acacia an extemporaneous mixture of syrup and mucilage of acacia would be preferable.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 306.

Lyons, A. B., points out that the synonym for syrup of lime, syrup of calcium hydroxide, is lacking in chemical exactness, as the calcium really exists as a sucrate.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 262.

Caldwell, Paul, believes that the syrup of ferrous iodide is injured by heat and recommends the addition of a small proportion of reduced iron to insure complete reaction. He also suggests the use of 0.1 per cent of citric acid as a preservative.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 220.

Wilbert, M. I., objects to the use of hypophosphorous acid as a preservative in the syrup of ferrous iodide, and points out that it is an ingredient not provided for in the protocol adopted by the International Conference at Brussels.—Am. J. Pharm., Phila., 1905, v. 77, p. 363.

Marquier, Adolph T., discusses syrup of hypophosphites and compound syrup of hypophosphites, and recommends that, in place of the latter preparation, a compound solution of hypophosphites, without sugar, after the formula of F. Sieker (Pharm. Rev.), be made official.—Proc. N. J. Pharm. Ass., 1905, pp. 80–82.

Fleet, F. W., calls attention to some of the shortcomings of the formula for compound syrup of hypophosphites and some of the difficulties that have been met with in its preparation. He points out the need for insisting on the use of pure chemicals.—Canad. Drug., 1905, v. 17, p. 179.

Stanislaus, I. V. S., objects to the use of acetic acid in syrup of ipecac, and suggests a modified formula containing ammonia water and an additional quantity of alcohol.—Am. Druggist, N. Y., 1905, v. 47, p. 351.

Caldwell, Paul, suggests the addition of about 5 per cent of glycerin in making syrup of krameria.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 306.

Caldwell, Paul, recommends that the full quantity of glycerin ordered in the formula for syrup of wild cherry, together with an equal quantity of water, be mixed with the wild cherry and allowed to macerate. He believes that the glycerin when used in this way not only extracts more of the coloring matter from the drug, but holds in solution more of the hydrocyanic acid.—*Ibid.*, p. 306.

Caldwell, Paul, says that glycerin, say 50 cc., might be included in the formula for compound syrup of squills; it prevents souring.—*Ibid.*, p. 306.

Caldwell, Paul, points out that no heat should be used in making syrup of tolu, as its odor, its lone peculiar property, is affected.—*Ibid.*, p. 306.

Fisk, Frank E., outlines a method for preparing syrup of tolu.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 394.

TAMARINDUS.

Adam, Franz (*Ztschr. d. österr. Apoth. Ver.*, 1905, v. 59, pp. 797–800), concludes that the acid present in tamarind is largely tartaric, partially in the form of an acid tartrate of potassium. There is also present an appreciable quantity of malic acid, some lactic acid, and a trace of volatile acids. Citric acid was not found.—*Just's Bot. Jahresb.* for 1905, v. 33, part 3, p. 189.

Maciel, Pérez M. (*Bol. Minist. Agric., Buenos Aires*, III, 2, pp. 110–113), discusses the cultivation of tamarind and its introduction into Argentine.—*Bot. Centralbl.*, 1905, v. 100, p. 268.

TARAXACUM.

Eberle, E. G., lists *Taraxacum officinalis* among the medicinal plants of Texas.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 305.

Havenhill, L. D., presents a general review of the literature relating to taraxacum, and gives an account of the chemical investigations on the composition and the possible uses of this drug.—*Western Drug-gist*, Chicago, 1905, v. 27, pp. 99–101.

The annual report by Philip Röder, Wien, records the examination of two samples of taraxacum. One contained 9.34 per cent of water and 3.63 per cent of ash, while the second contained 7.01 per cent of water and 31.50 per cent of ash. The second sample was found to be contaminated with upwards of 20 per cent of sand.—*Pharm. Post*, Wien, 1905, v. 38, p. 391.

Sayre, L. E., believes that the present process furnishes a good excipient, but not a preparation that properly represents the bitter and other medicinal constituents of the drug.—*Pharm. Era*, N. Y., 1905, v. 34, p. 173.

TEREBINTHINA CANADENSIS.

Rabak (*Pharm. Review*) asserts that the turpentine from *Abies amabilis* is used as a substitute for that from *Abies balsamea*. He enumerates the constants found, and gives a number of results obtained from the examination of the true as well as the spurious product.—*Pharm. Zentralh.*, 1905, v. 46, p. 689.

TEREBENUM.

Patch, Edgar L., reports finding one lot of terebene having a very dark color, another leaving 1.5 per cent of a dark residue, and a third which contained petroleum benzin.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 190.

TERPINI HYDRAS.

Siedler, P., points out that when terpin hydrate is dried according to the directions given in the German Pharmacopœia it does not melt, as required, at 116° C., but melts at 102° . The air dry substance melts at 116° , and this should have been stated in the pharmacopœia.—Pharm. Post., Wien, 1905, v. 38, p. 568.

Matzel, R., administered to himself up to 4 grammes of terpin hydrate without observing any effect whatsoever.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.-Nov., p. 88.

THYMOLIS IODIDUM.

Cormimboeuf, H., asserts that the commercial samples of thymol iodide are variable and may contain from 15 to 45 per cent of iodine. He outlines a method for the estimation of the contained iodine, as iodide of silver, by mixing the thymol iodide with sodium carbonate, heating to burn off the organic matter, dissolving, filtering the resulting solution, adding an excess of ammonia water and treating this solution with silver nitrate.—Ann. de chim. analyt., 1905, v. 10, pp. 453-454.

Kebler, Lyman F., reports finding a sample of thymol iodide containing 5.61 per cent of ash, 9.83 per cent of matter insoluble in ether, and 4.44 per cent of matter insoluble in chloroform.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 184.

The Committee on Drug Market reports that of 139 samples of thymol iodide, examined in Chicago, 23 were spurious, 66 were 20 per cent pure, 10 were 80 per cent pure, 9 were 90 per cent pure, and 31 were pure.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 183.

Waldmann (Apoth. Ztg., v. 19, p. 422) points out that a low-priced Swiss thymol iodide was found to contain only 50 per cent of dithymol diiodide: the other 50 per cent consisting of 30 per cent of salts soluble in water, calcium chloride and iodide, and 20 per cent insoluble matter, chiefly calcium carbonate. Another Swiss specimen contained only 15 per cent of dithymol diiodide and 85 per cent of red argillaceous earth. A German specimen was found which contained 30 per cent of dithymol diiodide, 13 per cent of water, and 57 per cent of insoluble added matter.—Year Book of Pharm., Lond., 1905, p. 24.

THYMOL.

Riedel's Berichte points out that the Ph. Germ., IV, requires a boiling point of from 228° to 230° for thymol, while Beilstein gives 231.8° as the boiling point for this substance. Experiments conducted by Riedel appear to indicate that the boiling point quoted by Beilstein is more nearly correct and that the figures given by the Ph. Germ., IV, are too low.—Riedel's Berichte, Berlin, 1905, p. 51.

TINCTURÆ.

Lyons, A. B., regrets that the tinctures of aconite root and of veratrum were made of "uniform" strength with that of other tinctures of potent drugs. Serious accidents are inevitable. We are committed to an official tincture so different from that to which physicians have become accustomed and which the majority of them will continue to use that the dispensing of either one in place of the other will jeopardize the welfare—possibly the life itself—of the patient. The 10 per cent tincture is *per se* much to be preferred to the 35 per cent one. It is interesting to note how arbitrarily changes in the strength of tinctures have been made in the direction of wholly unessential mathematical uniformity, regardless of the really important consideration of dose. Two mathematical considerations entered into the problem, viz, the percentage composition of the tincture and the dose. Of these the latter is quite as important as the former. If only one is to be retained, it should be the latter, so that the physician could learn once for all that the average dose of a tincture is a fluidrachm, or else that there are two classes of tinctures, the ordinary, with a dose of a fluidrachm, and the potent, dose one-fourth fluidrachm. This idea has been carried out in the Ph. Brit., IV, but it has been quite lost sight of in the present revision of the U. S. P. save that a vague distinction is made between potent (10 per cent) and ordinary (20 per cent) tinctures.

The tinctures of the U. S. P., VIII, are fairly satisfactory in mathematical uniformity, but how easily the whole class could be spared. One of the most important of all the tinctures, Tr. Iodi, although included in the international list of potent tinctures, has not been brought to the uniform 10 per cent standard, although, considering the presence in it of potassium iodide, it is probably as "strong" as a 10 per cent tincture would be.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 257.

Katz, J., points out that the object of tinctures and extracts is to present the active ingredients of a crude drug in a stable, unchanged form and, whenever possible, quantitatively representing all of the active ingredients of the original.—Chem. Repert. Cöthen, 1905, p. 200.

Herzog, G., discusses the several methods for extracting drugs in the production of tinctures and extracts, and reports a series of experiments made with the apparatus designed by Bruns, evidently a pressure percolator.—Ber. d. pharm. Gesellsch., 1905, v. 15, p. 107.

A symposium on the preparation of tinctures and extracts includes contributions by G. Arends, Berlin; W. Lenz, Berlin; W. Bruns, Elberfeld; and J. Herzog, Berlin.—*Ibid.*, pp. 124-159.

Tachiki, K., discusses the economical production of tinctures and the comparative value of the cold extraction and the percolation methods.—J. Pharm. Soc. Jap., Tokyo, 1905, p. 1.

Schaer, Eduard (Arch. Pharm., 1905, v. 243, pp. 198-217), discusses the influence of alkaline substances on spontaneous oxidation, and suggests that the darkening in color observed when pharmaceutical extracts are concentrated may be a consequence of the presence of ammonium nitrite, which Schönbein has shown to appear in water that is being evaporated. Besides effecting any specific oxidations characteristic of nitrites, it is one of those substances which accelerate auto-oxidation (its aqueous solution has an alkaline reaction).—J. Chem. Soc., Lond., 1905, v. 88, part 2, p. 434.

Panchaud, Adelbert, warns apothecaries that in the event of their buying tinctures and extracts they are responsible for their composition, and should test each lot for extractive, alcohol, and, whenever possible, the amount of active ingredient. He also points out that specific gravity, while an indication, is not conclusive. Color estimation may be of value. The estimation of extract content is best done by evaporation in aluminum dishes.—Schweiz. Wehnschr. f. Chem. u. Pharm., 1905, v. 43, p. 560.

Lucas and Dick (Pharm. J., Lond., 1905, v. 20, p. 362) present a comprehensive study, tabulated, of the specific gravity, percentage of extract and of alcohol present in the tinctures of the Ph. Brit., IV.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 597.

Hammer, J. W., discusses the extract content of tinctures.—Svensk Farm. Tidskr., 1905, v. 9, pp. 163-168.

Mohr, Charles, points out that, with the exception of the British, all pharmacopœias now in use make tinctures of dried substances correspond with the first dilution and so designate them; and, when the crude drug is the unit of strength, *all tinctures must of necessity be classed as dilutions*. . . . Most physicians have for years regarded, and still continue to regard, the tincture as the unit of strength, and they make the first dilution directly from the tincture in the proportion of 1 to 9.—Tr. Am. Inst. Homœop., 1905, v. 61, p. 60.

TRAGACANTHA.

Francis, John M., points out that when one purchases powdered tragacanth he has less protection than when he purchases the unground ribbons or tears, as a comparatively inferior tragacanth will produce quite a nice light-colored powder. He advises the rejection of tragacanth which has the slightest suggestion of bitterness, and to remember that only the best grades of tragacanth are suitable for emulsions and that the highest grade drug will be the most economical in the end.—Bull. Pharm., Detroit, 1905, v. 19, p. 452.

A communication to the committee on adulteration of the N. W. D. A. asserts that powdered tragacanth is frequently offered

mixed with more or less corn starch.—Paint. Oil and Drug. Rep., 1905, Oct. 6, p. 15.

The committee on adulteration reports finding one sample of powdered tragacanth which contained dextrin.—Proc. Michigan Pharm. Ass., 1905, p. 79.

Payet, M. E., outlines a test for powdered acacia in powdered tragacanth which depends on the brown color produced by the oxidase of the former when brought in contact with an aqueous solution of guaiacol in the presence of hydrogen dioxide.—Ann. de chim. analyt., 1905, v. 10, p. 63.

White, Edmund, points out that if mucilage of tragacanth be mixed with water and muscilage of acacia, respectively, the mixed muscilages are thinner than the corresponding mixture of tragacanth and water; . . . with other gums, like ghatti, which form glairy or viscous muscilages the same result does not appear to be obtained. He believes that the cause of this phenomenon is a problem which could very well be placed on the research list of the B. P. C.—Pharm. J., Lond., 1905, v. 21, p. 133.

TROCHISCI.

The editor believes that little change was called for in the official troches, because the preparation of lozenges has never been part of the art of the pharmacist, and the few combinations that have appeared in the various pharmacopœias have met with little appreciation at the hands of the medical profession. He also points out that compressed lozenges in this country have taken almost altogether the place of the confectioner's productions.—Drug Topics, 1905, v. 20, p. 217.

ULMUS.

Eberle, E. G., mentions *Ulmus fulva* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Vanderkleed, Charles E., found one sample of powdered elm bark which was grossly adulterated with starch.—Proc. Penna. Pharm. Ass., 1905, p. 54.

Havenhill, L. D., examined 9 samples of powdered elm bark. Two were found to contain traces of starch, and 2 additional samples contained a considerable quantity of wheat starch, and did not yield a satisfactory mucilage.—Proc. Kansas Pharm. Ass., 1905, p. 90.

Hommell, P. E., discusses the use of a glycerite of elm bark as a vehicle for a number of drugs, particularly insoluble substances such as bismuth subnitrate, and bismuth subcarbonate.—Proc. N. J. Pharm. Ass., 1905, pp. 59-61.

UNGUENTA.

Haenen, M., discusses the preparation of ointments, and insists on the need of having these preparations homogeneous. For the deter-

mination of the excellence of ointments, he recommends examining them by means of the compound microscope.—*J. de Pharm. d'Anvers.*, 1905, v. 61, p. 287.

Caldwell, Paul, asserts that the formula for the ointment of rose water can be improved by replacing 25 grammes of the spermaceti with a corresponding quantity of white wax and increasing the almond oil to the quantity official in the U. S. P., 1890.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 307.

A contributor asserts that diachylon ointment should be kept in a cool place, and not used after from six to eight weeks.—*Pharm. Post, Wien*, 1905, v. 38, p. 777.

Caldwell, Paul, asserts that diachylon ointment of the U. S. P., VIII, is softer than it should be, and recommends 60 grammes of lead plaster to 39 grammes of olive oil.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 307.

Caldwell, Paul, asserts that nutgall ointment does not keep well, "a fungus growth forming around the sides of its container," and recommends the addition of 2 per cent of boric acid.—*Ibid.*, p. 307.

UNGUENTUM HYDRARGYRI.

The annual report of Philip Röder, Wien, outlines a method for the analysis of mercurial ointment which is designated as a modification by Firbas of Glückmann's method.—*Pharm. Post, Wien*, 1905, v. 38, p. 393.

Eberle, E. G., points out that mercurial ointment may be assayed by taking a test tube, filling it to within about one-fourth of the top with a solution of magnesium sulphate (1-2) then adding a weighed portion of the ointment. Place the tube in a water bath until the ointment is melted. The mercury settles to the bottom and the grease floats on top. Then cool, insert a glass rod and place the mixture in an ice bath. The ointment will congeal around the inserted tube and can, by means of it, be removed; decant the liquid and wash, dry, and weigh the mercury.—*Apothecary, Boston*, 1905, v. 17, p. 951.

Wetterstroem, Theo. D., asserts that mercurial ointment frequently contains petrolatum instead of lard.—*Drug. Circ. & Chem. Gaz.*, N. Y., 1905, v. 49, p. 312.

UNGUENTUM HYDRARGYRI AMMONIATI.

Caldwell, Paul, suggests the following directions for the preparing of the ointment of ammoniated mercury:

Warm the hydrous wool fat, add the ammoniated mercury and force the mixture through a number 60 sieve; melt the white petroleum and pass it through the sieve; then transfer the container and content to an ice bath and stir until cold.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 307.

UNGUENTUM HYDRARGYRI NITRATIS.

Snavelly, Clarence O., suggests a modification of the official formula and process which he believes has the advantage of insuring a definite solution of mercuric nitrate, without any mercurous salt, and a product having less odor.—*Am. J. Pharm., Phila.*, 1905, v. 77, pp. 233-239.

UNGUENTUM HYDRARGYRI OXIDI FLAVI.

An abstract discusses the several methods that have been proposed for making Pagenstecher's ointment and suggests that the 2 per cent ointment be included in the next *Ph. Germ.*—*Pharm. Ztg., Berlin*, 1905, v. 50, p. 686.

Sturmer, J. W., believes that the presence of water in an ointment made with freshly precipitated mercuric oxide, is objectionable and therefore recommends that the water be washed out with alcohol, and the latter with ether. Before the ether has evaporated entirely he mixes the mercuric oxide with the desired ointment base to make a 50 per cent stock ointment, which he dilutes as needed.—*Apothecary, Boston*, 1905, v. 17, p. 951.

UNGUENTUM HYDRARGYRI OXIDI RUBRI.

Raubenheimer, Otto, suggests the following formula for the preparation of a permanent ointment of red mercuric oxide. Red mercuric oxide, 10 gm.; castor oil, 5 gm.; petroleum, 85 gm.; mix. The finished ointment he recommends keeping in a jar under about 1 inch of water.—*Am. Druggist, N. Y.*, 1905, v. 47, p. 200.

UNGUENTUM POTASSII IODIDI.

Caldwell, Paul, suggests—

Substituting potassium carbonate for sodium hyposulphite is not an improvement. The alkalies tend to liquefy the lard and thus make the ointment soft. If hydrous wool fat and white petrolatum were the base, no doubt this difficulty would be overcome.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 307.

UNGUENTUM ZINCI OXIDI.

Magoffin, A. E., suggests the use of enough glycerin, in the formula for the ointment of zinc oxide, to make a paste with the zinc oxide before adding the petroleum.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 346.

Caldwell, Paul, recommends mixing two-thirds of the lard, previously melted, with the zinc oxide and running the mixture through a number 60 sieve into a suitable dish immersed in ice water. Heat the remainder of the lard and pass this through the sieve into the

first portion of the ointment, stir well, until cool.—Drug. Circ. & Chem. Gaz., N. Y., 1905, v. 49, p. 220.

VIRUS VACCINICUM.

von Prowazek, S., discusses the several views advanced with regard to the nature of vaccine and reports a study of the character of structures found in the virus. He also reports a study of the structural changes produced in the skin of the calf infected with vaccine virus.—Arb. a. d. K. Gesundheitsamte, 1905, v. 22, pp. 525–541.

Warfield, Louis M., reports a case of erythema multiforme following vaccination.—J. Am. M. Ass., 1905, v. 45, p. 852.

An editorial discusses vaccination during the eruptive stage of smallpox.—*Ibid.*, p. 723.

VALERIANA.

The annual report of Philip Röder, Wien, records the examination of a sample of valerian which yielded 8.86 per cent of water and 10.42 per cent of ash.—Pharm. Post, Wien, 1905, v. 38, p. 391.

Kionka, H. (Arch. internat. de Pharmacod. et de Thérap, 1905, v. 15, p. 279), reports experiments with various kinds of valerian. He believes that the content of oil is the important factor and that this is dependent on soil conditions.—Biochem. Centralbl., 1905, v. 4, p. 452.

Gadd, H. Wippell and Sydney C., assert that valerian should not yield more than 9 per cent of ash; they also propose a solid extract standard (3 per cent) for the ammoniated tincture of valerian of the Ph. Brit.—Pharm. J., Lond., 1905, v. 21, p. 520.

VANILLA.

Hennings, R., discusses the economic conditions prevailing in the drug market, relating to vanilla, and enumerates the chief sources of supply for Germany.—Der Tropenpflanzer, Berlin, 1905, v. 9, pp. 87–89.

An abstract from a paper by J. H. Dow (Bull. Pharm.) describes some of the tricks resorted to, in connection with vanilla beans, and cautions against the use of manipulated beans.—Canad. Druggist, 1905, v. 17, p. 178.

Caeser and Loretz discuss the several varieties of vanilla now on the market. They appear to regard the Bourbon bean as being the most desirable, with the Comoro, Seychelles, and Madagascar varieties as being closely allied to the former.—Geschäfts-Ber. von Caeser & Loretz, in Halle a. S., 1905, p. 37.

Spaeth, E., points out that the generally accepted definitions for vanilla are not satisfactory. Sufficient data are not included for the recognition of the cheaper grades of vanilla and vanillons. The

adulteration with benzoic acid and the coating with oil or balsam of Peru should be taken into consideration. The addition of vanillin to vanilla beans is not uncommon and should be considered as an adulteration. Commercially acceptable vanilla should consist of the unripe, closed brownish-black fruit of *Vanilla planifolia* Andrews. It should have an agreeable odor and taste and should not be wholly or partially extracted. Cracked, thin, yellowish brown, or stiff fruit having the characteristic heliotrope odor should not be accepted. The amount of ash should not exceed 5 per cent.—Ztschr. f. Unters. d. Nahr. u. Genusssm., 1905, v. 10, p. 32.

Hanus, J., reviews the efforts to develop a satisfactory method for the quantitative estimation of vanillin in vanilla and preparations of vanilla, and outlines a process depending on the use of nitrobenzhydrazine as a precipitant.—Ztschr. f. Unters. d. Nahr. u. Genusssm., 1905, v. 10, p. 585.

An abstract (from Revue internat. des falsificat., 1905) outlines the methods that have been adopted for the curing of vanilla in the Seychelles and on the Island of Reunion. Also records some analytical data as to different varieties of vanilla.—Pharm. Zentralh., 1905, v. 46, p. 688.

The Bureau of Plant Industry reports experiments on the growing and maturing of vanilla beans. A sufficient crop was matured to carry the product through the fermentation process and produce the article in a commercial condition.—Ann. Rep. Dept. Agric., 1905, p. 97.

Inkersley, A. (from World To-Day, v. 9, pp. 1012-1013), gives an account of planting about 8,000 cuttings of vanilla in the region of Kona, Hawaii, where it is believed the climate is especially suitable for this crop.—Exp. Sta. Rec., v. 17, p. 563.

Jackson, J. R. (in Gardner's Chronicle), notes some curious facts regarding vanilla cultivation in Tahiti and Mauritius.—Bull. Dept. Agric., Jamaica, 1905, v. 3, pp. 70-71 (April).

Just's Botanischer Jahresber. (1905, v. 33, part 3, pp. 752-753) contains several additional references relating to the cultivation and curing of vanilla.

Caldwell, Paul, believes that the odor of the finished tincture of vanilla is seriously affected by having come in contact with iron during any stage of its making. He deprecates the grinding of the bean in an iron mortar, with sand or glass, and particularly cautions against the use of a rusty iron percolator.—Drug. Circ. & Chem. Gaz., 1905, v. 49, p. 220.

Winton and Bailey discuss the adulteration of vanillin with acetanilide, and outline a method for determining vanillin, coumarin, and acetanilide in vanillin, vanilla, and vanilla extract.—J. Am. Chem. Soc., 1905, v. 27, pp. 719-724.

Caeser and Loretz announce that they prepare a 1 to 9 mixture of vanilla with cane sugar that will serve as a flavoring ingredient in place of the widely used essence or tincture of vanilla.—Geschäfts-Ber. von Caesar & Loretz, in Halle a. S., 1905, p. 19.

VANILLINUM.

An editorial characterizes vanillin—

As rather a strange addition to the pharmacopœia, as it has no medicinal use and does not enter into any official pharmaceutical product.—Drug Topics, 1905, v. 20, p. 199.

Schimmel & Co. assert that adulteration of vanillin is still carried on extensively. A sample recently examined proved to consist of at least 50 per cent of terpin hydrate. The terpin hydrate isolated was recognized by its melting point, and by the fact that the odor of terpineol occurred when it was heated with dilute sulphuric acid.—Semi-Ann. Rep., Schimmel & Co., 1905, Apr.–May, p. 120.

Fitzgerald, Francis A. J., refers to the production of vanillin by the oxidation of eugenol by means of ozone, thus obviating the secondary products or disturbing influences that are possible by the use of other oxidizing agents.—Ztschr. f. angew. Chem., 1905, v. 18, p. 1743.

An abstract from La Revue des produits chimiques discusses the method of preparing vanillin and protocatechuic aldehyde from isosafrol.—Paint, Oil, and Drug Rep., 1905, Aug. 28, p. 40.

Rosenthaler, L., discusses the color reactions that take place with substances of the ketone class and with a number of essential oils. The latter he classifies in four groups, as they produce green, violet, blue, or bluish green colorations.—Ztschr. f. analyt. Chem., 1905, v. 44, pp. 292–301.

Kutscheroff, M., discusses the so-called vanillin reaction of the ketones and points out a number of imperfections and shortcomings.—*Ibid.*, p. 622.

Hartwich and Winckel (Arch. d. Pharm.) show that a large number of phenols (and tanning substances) give definite color reactions with a solution of vanillin in hydrochloric acid, in the cold and when heated.—Semi-Ann. Rep., Schimmel & Co., 1905, Oct.–Nov., p. 111.

La Wall, Charles H., discusses the behavior of vanillin toward the formaldehyde tests and presents a tabulated record of a number of experiments. He points out that under some conditions vanillin is liable to be mistaken for formaldehyde.—Proc. Pennsylvania Pharm. Ass., 1905, pp. 200–202.

Kastle, J. H., outlines a simple method for distinguishing between coumarin and vanillin. The reagent used is a mixture of 5 cc. of phenol and 5 cc. of pure concentrated sulphuric acid.—Bull. No. 26, Hyg. Lab., U. S. P. H. and M.-H. S., pp. 33–35.

Kotake, Y. (Ztschr. f. physiol. Chem., v. 45, pp. 320-325), discusses the fate of vanillin in the animal body. He found a laevo-rotatory substance in the urine, and describes some experiments made with it.—Jahresber. for, 1905, ü. d. Fortschr. d. Tier-Chem. Wiesb., v. 35, p. 127.

VERATRINA.

The official title for veratrine, in the Netherlands Pharmacopœia is "Cevadinum" with "Veratrinum crystallisatum" as a synonym.—Pharmacopœia Nederlandica, 1905, p. 79.

Reichard, C., presents a compilation of the several reactions and tests suggested as being characteristic for the alkaloid of *Sabadilla officinalis*.—Pharm. Zentralh. 1905, v. 46, p. 644.

VERATRUM.

The revisors of Vienna Pharmacies found hellebore root to have been mistaken for Rad. Veratri viridi, and point out that the cause for this is no doubt to be found in the common German name "Nieswurz" for both of these drugs.—Pharm. Prax., 1905, v. 4, p. 38.

Beringer, Geo. M., believes that the reduction in drug strength of this preparation has minimized its action, as the alcohol present is sufficient to overbalance the drug action. He does not approve of the recognition of both hellebores under one title. The identity of the two plants, either botanically or as to chemical constituents, is not satisfactorily established.—Proc. Am. Pharm. Ass., 1905, v. 53, pp. 414-415.

Remington, J. P., points out that there need be no concern because the U. S. P. VIII recognizes both *Veratrum viride* and *Veratrum album*.

The pharmacopœia committee were advised that investigation had shown that *Veratrum album* possesses properties equivalent to those of *Veratrum viride*.

But as the text of the pharmacopœia stands it does not prevent the making of preparations from *Veratrum viride*.—*Ibid.*, p. 254.

VIBURNUM OPULUS.

Lloyd, John Uri, points out that *Viburnum opulus* was employed long before *Viburnum prunifolium* was introduced and came to be known under the name viburnum. The introduction of prunifolium complicated the matter, and in order that there might be no confusion he suggests that the name "black haw" be used for *Viburnum prunifolium*.—Pharm. Rev., 1905, v. 23, p. 333.

VIBURNUM PRUNIFOLIUM.

Eberle, E. G., lists *Viburnum prunifolium* among the medicinal plants of Texas.—Proc. Am. Pharm. Ass., 1905, v. 53, p. 305.

Lloyd, John Uri, asserts that the bark of all species of wild haw native to the country that supplies the drug for the market is collected by root diggers and sold under the name "black haw."—*Pharm. Rev.*, 1905, v. 23, p. 333.

VINA.

Nixon, C. F., asserts that *Vinum Album* and *Vinum Rubrum* are left in a more unsatisfactory condition, if possible, than in the preceding revision of the U. S. P. There is nothing to indicate, except by analysis, what wines should be used. Native Riesling corresponds most nearly to "Whitewine" and native Burgundy to "Red Wine," but neither is in general use or much known.—*Apothecary*, Boston, 1905, v. 17, p. 774.

Gayon, U., discusses the preparation and the preserving of wine.—*Bull. Soc. de Pharm. de Bordeaux*, 1905, v. 45, pp. 301-318.

Kebler, Lyman F. (quoting from *Bull. Health Dept. Cal.*), asserts that 12 samples of wine contained arsenic, 1 arsenic and benzoic acid, 2 arsenic and coal-tar dyes, 2 salicylic acid and coal-tar dyes, and 5 salicylic acid, 5 benzoic acid, 8 coal-tar dye, and 1 aluminum, benzoic acid, and coal-tar dye.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 190.

Wilbert, M. I., objects to the continuance of wine as a menstruum for pharmaceutical preparations, because of its variability and generally unsatisfactory nature as a solvent, and recommends conforming more closely to the recommendations of the International Conference for the Unification of the Formulae of Potent Remedies.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, pp. 405-407.

The Spanish Pharmacopœia includes formulas for 15 wines. The only distinctly potent wine, apart from the wine of antimony, which is called "*Vinum emeticum*, *Vinum antimoniale seu stibiatum*," is the "*Vinum opii compositum*," the old-time Sydenham's laudanum.—*Pharmacopea Oficial Española*, 1905, pp. 612-620.

Kramszky, Ludwig, discusses the presence of tannin in wines, and proposes a method for estimating the amount present. He concludes that ammoniacal zinc sulphate solution will precipitate tannin. The normal constituents of wine do not influence this precipitation.—*Ztschr. f. analyt. Chem.*, 1905, v. 44, pp. 756-765.

Caldwell, Paul, points out that, in the preparing of the wine of iron and the bitter wine of iron, the wine should be detannated so as to avoid the formation of the unsightly and insoluble tannate of iron.—*Drug. Circ. & Chem. Gaz.*, 1905, v. 49, p. 307.

ZINCI CHLORIDUM.

Mylius and Dietz report some experiments made to determine the solubility of zinc chloride.—*Ber. d. deuts. chem. Gesellsch.*, 1905, v. 38,

pp. 921-923. With additional details of methods and results, and several charts.—*Ztschr. f. anorgan. Chem.*, 1905, v. 44, pp. 209-220.

The annual report by Philip Röder, Wien, points out that zinc chloride is sometimes met with which does not comply with the solubility requirement.—*Pharm. Post. Wien*, 1905, v. 38, p. 393.

Copeland, Royal S., suggests a 1:500 solution of zinc chloride in water as being useful in the treatment of pink-eye.—*Hahneman. Month., Phila.*, 1905, p. 318.

McClintic, T. B., reviews the literature relating to the properties and uses of zinc chloride, and discusses the possible uses of this compound as a deodorant, an antiseptic, and a germicide. He concludes that, while zinc chloride has some properties as a deodorant to recommend it favorably, its antiseptic and germicidal powers are comparatively feeble, and this fact, with its cost and caustic properties, practically exclude it from the useful and reliable disinfectants.—*Bull. No. 22, Hyg. Lab. U. S. P. H. & M.-H. S. Wash.*, 1905, p. 24.

ZINCI OXIDUM.

The committee on adulteration points out that zinc oxide is quite often found to contain chlorides and sulphates, and occasionally iron.—*Proc. Michigan Pharm. Ass.*, 1905, p. 79.

The annual report by Philip Röder, Wien, indicates that lead is a frequent contamination of zinc oxide. Of three samples examined, two were refused because of their lead content, which was demonstrated by a process suggested by Glückmann: Dissolving the zinc oxide in acetic acid and treating this with potassium dichromate.—*Pharm. Post, Wien*, 1905, v. 38, p. 393.

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ZINCI SULPHAS.

The annual report of Philip Röder, Wien, says that of five samples of zinc sulphate examined, three were found to be contaminated with iron and aluminum.—*Pharm. Post, Wien*, 1905, v. 38, p. 393.

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ZINGIBER.

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Kebler, Lyman F., reports that a sample of ginger extract that was shown to be made with wood alcohol caused the death of one person.—*Proc. Am. Pharm. Ass.*, 1905, v. 53, p. 184.

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LIST OF HYGIENIC LABORATORY BULLETINS OF THE PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.

The Hygienic Laboratory was established in New York, at the Marine Hospital on Staten Island, August, 1887. It was transferred to Washington, with quarters in the Butler Building, June 11, 1891, and a new laboratory building located in Washington, was authorized by act of Congress, March 3, 1901.

The following *bulletins* [Bulls. Nos. 1-7, 1900 to 1902, Hyg. Lab., U. S. Marine-Hosp. Serv., Wash.] have been issued:

* No. 1.—Preliminary note on the viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 2.—Formalin disinfection of baggage without apparatus. By M. J. Rosenau.

* No. 3.—Sulphur dioxid as a germicidal agent. By H. D. Geddings.

* No. 4.—Viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 5.—An investigation of a pathogenic microbe (*B. typhi murium* Danyz) applied to the destruction of rats. By M. J. Rosenau.

* No. 6.—Disinfection against mosquitoes with formaldehyd and sulphur dioxid. By M. J. Rosenau.

No. 7.—Laboratory technique: Ring test for indol, by S. B. Grubbs and Edward Francis; Collodium sacs, by S. B. Grubbs and Edward Francis; Microphotography with simple apparatus, by H. B. Parker.

By act of Congress approved July 1, 1902, the name of the "United States Marine-Hospital Service" was changed to the "Public Health and Marine-Hospital Service of the United States," and three new divisions were added to the Hygienic Laboratory.

Since the change of name of the Service the bulletins of the Hygienic Laboratory have been continued in the same numerical order, as follows:

* No. 8.—Laboratory course in pathology and bacteriology. By M. J. Rosenau. (Revised edition, March, 1904.)

* No. 9.—Presence of tetanus in commercial gelatin. By John F. Anderson.

No. 10.—Report upon the prevalence and geographic distribution of hookworm disease (uncinariasis or ancylostomiasis) in the United States. By Ch. Wardell Stiles.

* No. 11.—An experimental investigation of *Trypanosoma lewisi*. By Edward Francis.

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* No. 18.—An account of the tapeworms of the genus *Hymenolepis* parasitic in man, including reports of several new cases of the dwarf tapeworm (*H. nana*) in the United States. By Brayton H. Ransom.

* No. 19.—A method for inoculating animals with precise amounts. By M. J. Rosenau.

* No. 20.—A zoological investigation into the cause, transmission, and source of Rocky Mountain "spotted fever." By Ch. Wardell Stiles.

No. 21.—The immunity unit for standardizing diphtheria antitoxin (based on Ehrlich's normal serum). Official standard prepared under the act approved July 1, 1902. By M. J. Rosenau.

* No. 22.—Chloride of zinc as a deodorant, antiseptic, and germicide. By T. B. McClintic.

* No. 23.—Changes in the Pharmacopœia of the United States of America. Eighth Decennial Revision. By Reid Hunt and Murray Galt Motter.

No. 24.—The International Code of Zoological Nomenclature as applied to medicine. By Ch. Wardell Stiles.

No. 25.—Illustrated key to the cestode parasites of man. By Ch. Wardell Stiles.

No. 26.—On the stability of the oxidases and their conduct toward various reagents. The conduct of phenolphthalein in the animal organism. A test for saccharin, and a simple method of distinguishing between cumarin and vanillin. The toxicity of ozone and other oxidizing agents to lipase. The influence of chemical constitution on the lipolytic hydrolysis of ethereal salts. By J. H. Kastle.

No. 27.—The limitations of formaldehyde gas as a disinfectant with special reference to car sanitation. By Thomas B. McClintic.

* No. 28.—A statistical study of the prevalence of intestinal worms in man. By Ch. Wardell Stiles and Philip E. Garrison.

* No. 29.—A study of the cause of sudden death following the injection of horse serum. By M. J. Rosenau and John F. Anderson.

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No. 33.—Studies in experimental alcoholism. By Reid Hunt.

No. 34.—I. *Agamofilaria georgiana* n. sp., an apparently new roundworm parasite from the ankle of a negress. II. The zoological characters of the roundworm genus *Filaria* Mueller, 1787. III. Three new American cases of infection of man with horsehair worms (species *Paragordius varius*), with summary of all cases reported to date. By Ch. Wardell Stiles.

* No. 35.—Report on the origin and prevalence of typhoid fever in the District of Columbia. By M. J. Rosenau, L. L. Lumsden, and Joseph H. Kastle. (Including articles contributed by Ch. Wardell Stiles, Joseph Goldberger, and A. M. Stimson.)

No. 36.—Further studies upon hypersusceptibility and immunity. By M. J. Rosenau and John F. Anderson.

No. 37.—Index-catalogue of medical and veterinary zoology. Subjects: Trematoda and trematode diseases. By Ch. Wardell Stiles and Albert Hassall.

No. 38.—The influence of antitoxin upon post-diphtheritic paralysis. By M. J. Rosenau and John F. Anderson.

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*No. 41.—Milk and its relation to the public health. By various authors.

No. 42.—The thermal death points of pathogenic micro-organisms in milk. By M. J. Rosenau.

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No. 46.—*Hepatozoon perniciosum* (n. g. n. sp.): a haemogregarine pathogenic for white rats; with a description of the sexual cycle in the intermediate host, a mite (*Lelaps echidninus*). By W. W. Miller.

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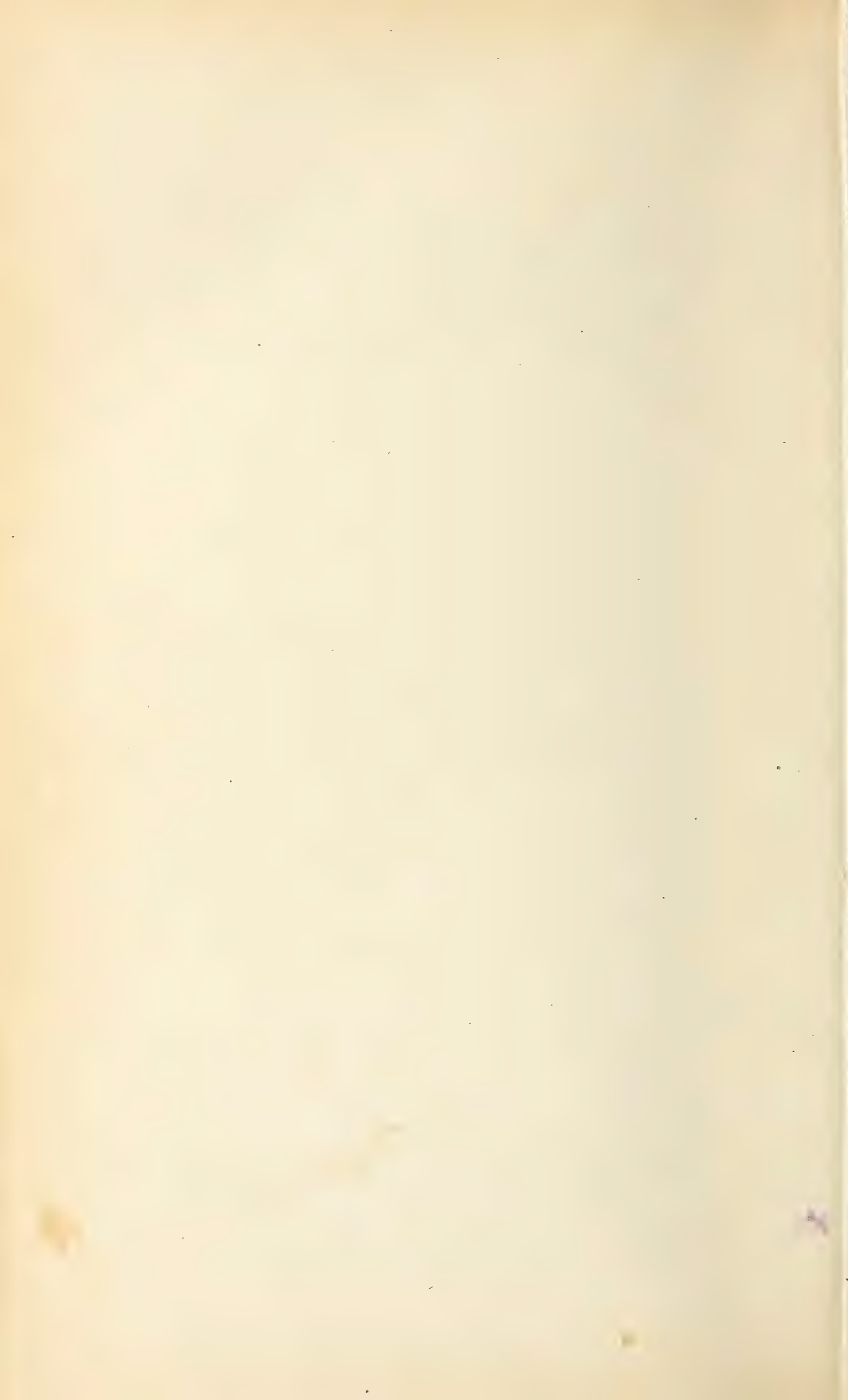
No. 49.—Digest of Comments on the Pharmacopœia of the United States of America, Eighth Decennial Revision, for the period ending December 31, 1905. By Murray Galt Motter and Martin I. Wilbert.

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Public Health and Marine-Hospital Service of the United States

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APRIL, 1909

FURTHER STUDIES UPON THE PHENOMENON
OF ANAPHYLAXIS

By

M. J. ROSENAU

and

JOHN F. ANDERSON



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CONTENTS.

	Page.
Introduction.....	7
Influence of hypnotics.....	8
Urethane.....	9
Chloral.....	9
Paraldehyde.....	11
Magnesium sulphate.....	12
Specificity.....	20
Effect of heat on the toxicity of proteins.....	22
Effect of heat upon the sensitizing property of proteins.....	30
Effect of heat upon sensitive guinea-pig serum.....	37
Sensitizing action of dried horse serum.....	38
Sensitizing action of euglobulins.....	39
Immunity.....	40
Antibodies.....	42
Time.....	47
Summary and conclusions.....	48

FURTHER STUDIES UPON THE PHENOMENON OF ANAPHYLAXIS.^a

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Studies upon anaphylaxis, both in this country and abroad, indicate that the phenomenon has an important bearing upon certain fundamental problems in medicine.

A satisfactory explanation of the intimate nature of anaphylaxis would doubtless give us a much better understanding of a large class of diseases. The close relationship between anaphylaxis and immunity is evident. Advances in our knowledge of the former will surely lead to practical progress in the latter.

There appears to be much similarity between anaphylaxis and the processes that take place in tuberculosis. Diseases like hay fever find their explanation in a specific hypersusceptibility. The serum disease, following the introduction of alien proteins and the hypersusceptibility that some persons display to certain proteins when ingested, are frequent clinical instances of anaphylaxis, the manifestations of which are multiple and various.

We shall doubtless know more about the endotoxins, the period of incubation of disease, protein metabolism, and other obscure problems in pathology, when we know more about the phenomenon of anaphylaxis. These and other practical bearings of the subject have been dwelt upon by us in a recent lecture before the Harvey Society.^b

^a Manuscript submitted for publication April 5, 1909.

^b Arch. Internal Med., April, 1909 (in press).

In order to obtain a deeper insight into anaphylaxis and its varied bearings, we consider that a study of the phenomenon itself is of first importance and we have been engaged upon this phase of the subject since 1906.^a These studies have mostly been made upon guinea pigs.

We have, therefore, devoted most of our attention to a study of the intimate nature of the factors that make up the phenomenon of anaphylaxis, subordinating, for the time being, discussions of the theory of its mechanism or its practical application.

INFLUENCE OF HYPNOTICS.

Following the work of Besredka upon the influence of ether upon the development of anaphylaxis, Banzhaf and Famulener^b reported interesting observations upon the prevention of anaphylaxis by the previous administration of chloral hydrate. They found that if sensitive guinea pigs be given large doses of chloral hydrate intramuscularly, sufficient to render them completely narcotized, and then given an injection of serum, death from anaphylaxis was prevented in a large percentage of cases.

This procedure appeared to us to be theoretically a very promising one. It has seemed to us, as well as to others, that death from anaphylaxis was due perhaps to an overstimulation of probably the respiratory center, and if the affected center could be so blunted that it would not respond to this extreme stimulation perhaps the animal might be tided over the critical period and recover.

If this should be found to be true perhaps it would be of use when it is found necessary to administer antitoxin to persons suspected, before hand, of being susceptible to an injection of horse serum; as, for example, asthmatics or persons who experience discomfort when in the neighborhood of horses.

We therefore made a number of experiments with various hypnotics to determine their influence upon anaphylaxis. In one series we gave sensitive guinea pigs different amounts of urethane by the mouth and when the narcosis was complete they were tested for their susceptibility by an injection of horse serum.

As will be seen from the table (No. 1), the urethane had but slight effect upon the subsequent development of anaphylaxis.

^a Rosenau, M. J., and Anderson, John F.: A study of the cause of sudden death following the injection of horse serum. Hyg. Lab. Bul. No. 29, 1906.

Further studies upon hypersusceptibility, Hyg. Lab. Bul. No. 36, 1907.

Further studies upon anaphylaxis, Hyg. Lab. Bul. No. 45, 1908.

^b Proc. Soc. Exper. Biol. and Med., N. Y., vol. 5, 1908, p. 62.

TABLE No. 1.—*Urethane*.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10123.....	510	0.23 c. c. toxine no. 7+1/460 c. c. antitoxic horse serum (NYBH 10B).	86	1 gm. urethane by mouth 45 minutes later, complete narcosis, 6 c. c. normal horse (Teddy) serum, intraperitoneally.	Dead in 3 hours.
10105.....	530	0.23 c. c. toxine no. 7+1/380 c. c. antitoxic horse serum (NYBH 10B).	86do.....	Dead in 75 minutes.
10155.....	500	0.23 c. c. toxine no. 7+1/540 c. c. antitoxic horse serum (NYBH 13C).	86	0.9 gm. urethane by mouth, 70 minutes later, complete narcosis, 6 c. c. normal (Frank) serum intraperitoneally.	Dead in 30 minutes.
10156.....	465	0.23 c. c. toxine no. 7+1/520 c. c. antitoxic horse serum (NYBH 13C).	86do.....	Masked symptoms, recovered.

TABLE No. 2.—*Urethane*.

[Controls—toxic dose.]

G. P. No.	Weight.	Inoculation.	Result.
	<i>Grams.</i>		
Control....	535	1 gm. urethane by mouth, complete narcosis.....	Recovered.
Do.....	410	1.5 gm. urethane by mouth, complete narcosis....	Dead in 2 hours 15 minutes
Do.....	415	1 gm. urethane by mouth, complete narcosis.....	Dead in 7 hours.
Do.....	410	0.9 gm. urethane by mouth, complete narcosis....	Dead in 33 hours.
Do.....	475do.....	Recovered.
Do.....	415	0.8 gm. urethane by mouth, complete narcosis....	Do.
Do.....	420	0.7 gm. urethane by mouth, complete narcosis....	Do.

CHLORAL.

In Table No. 3 will be seen the results of the use of chloral for the prevention of anaphylaxis.

While the amounts, in most cases, were not sufficient to render the animal absolutely insensible to pain, the narcosis was very deep; but, in spite of it, practically all the animals died from the second injection of serum.

TABLE NO. 3.—*Chloral*.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10138.....	500	0.23 c. c. toxine, 7+1/580 c. c. antitoxic horse serum (NYBH 13C).	86	200 mg. chloral, 5 per cent solution, into muscles of both thighs. 120 minutes later, narcosis not complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Marked symptoms, recovered.
10139.....	500	0.23 c. c. toxine, 7+1/580 c. c. antitoxic horse serum (NYBH 13C).	86do.....	Dead in 20 minutes.
10154.....	520	0.23 c. c. toxine, 7+1/540 c. c. antitoxic horse serum (NYBH 13C).	86do.....	Dead in 25 minutes.
10127.....	570	0.23 c. c. toxine, 7+1/420 c. c. antitoxic horse serum (NYBH 10B).	88	250 mg. 5 per cent solution of chloral into muscles of both thighs. 30 minutes later, narcosis complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Symptoms, recovered.
10142.....	580	0.23 c. c. toxine, 7+1/540 c. c. antitoxic horse serum (NYBH 13C).	88do.....	Do.
10143.....	590do.....	88do.....	Do.
10103.....	540	0.23 c. c. toxine, 7+1/400 c. c. antitoxic horse serum (NYBH 10B).	92	200 mg. 5 per cent chloral solution into muscles of both thighs. 21 minutes later, narcosis almost complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Dead in 40 minutes.
10100.....	485	0.23 c. c. toxine, 7+1/420 c. c. antitoxic horse serum (NYBH 10B).	92	200 mag. 5 per cent chloral solution into muscles of both thighs. 30 minutes later, narcosis almost complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Dead in 25 minutes
10104.....	520	0.23 c. c. toxine, 7+1/380 c. c. antitoxic horse serum (NYBH 10B).	92	200 mg. 5 per cent chloral solution into muscles of both thighs. 31 minutes later, narcosis almost complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Dead in 60 minutes
10107.....	505	0.23 c. c. toxine, 7+1/360 c. c. antitoxic horse serum (NYBH 10B).	92	200 mg. 5 per cent chloral solution into muscles of both thighs 32 minutes later, narcosis almost complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Dead in 90 minutes.

TABLE No. 3.—*Chloral*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
10113.....	<i>Grams.</i> 490	0.23 c. c. toxine, 7+1/440 c. c. antitoxic horse serum (NYBH 10B).	92	200 mg. 5 per cent chloral solution into muscles of both thighs. 22 minutes later, narcosis almost complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Recovered.

TABLE No. 4.—*Chloral*.

[Controls—toxic dose.]

G. P. No.	G. P. weight.	Injection.	Result.
Control....	<i>Grams.</i> 420	125 mg. 5 per cent chloral solution into muscles of both thighs, complete narcosis.	Recovered.
Do.....	425	150 mg. 5 per cent chloral solution into muscles of both thighs, complete narcosis.	Do.
Do.....	425	175 mg. 5 per cent chloral solution into muscles of both thighs, complete narcosis.	Do.
Do.....	470	200 mg. 5 per cent chloral solution into muscles of both thighs, complete narcosis.	Do.
Do.....	550	250 mg. 5 per cent chloral solution into muscles of both thighs, complete narcosis.	Do.

PARALDEHYDE.

Some experiments were made (Table No. 5) with paraldehyde for the same purpose; but it appeared to have but slight influence

TABLE No. 5.—*Paraldehyde*.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
10153.....	<i>Grams.</i> 405	0.23 c. c. toxine, 7+1/560 antitoxic horse serum (NYBH 13C).	86	1 c. c. paraldehyde by mouth. 1 hour later, narcosis not quite complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Markedsymptoms, recovered.
10137.....	465	0.23 c. c. toxine, 7+1/480 c. c. antitoxic horse serum (NYBH 13C).	86	1 c. c. paraldehyde by mouth. 1 hour later, narcosis complete, 6 c. c. normal horse (Frank) serum intraperitoneally.	Dead in 16 minutes.

TABLE No. 5.—*Paraldehyde*—Continued.

G. P. No.	G. P. weight.	Injection.	Result.
	<i>Grams.</i>		
Control.....	385	0.9 c. c. paraldehyde by the mouth, narcosis complete.....	Recovered.

MAGNESIUM SULPHATE.

The experiments of Meltzer with the use of magnesium sulphate as an anæsthetic prompted us to make some experiments with this substance for the prevention or modification of anaphylaxis. These experiments varied in several particulars.

In one series (Table No. 6) sensitive guinea pigs were given sufficient magnesium sulphate subcutaneously to render them completely anæsthetic, and then they were given an injection of horse serum containing sufficient calcium chloride in solution to counteract the effect of the magnesium sulphate.

In another series the animals were given the same treatment, except that no calcium chloride was included in the serum.

Another series was given the magnesium sulphate; then, when the narcosis was complete, they were given calcium chloride subcutaneously and within one or two minutes given the injection of serum.

Others were given magnesium sulphate, then the serum and, before symptoms appeared, the calcium chloride.

It will be seen from the results in the tables that none of these procedures seem to exert any favorable influence upon the final result.

TABLE No. 6.—*Magnesium sulphate, then calcium chloride dissolved in horse serum.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
11060.....	475	0.23 c. c. toxine 7+1/300 c. c. antitoxic horse serum (LB 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 43 minutes later, narcosis complete, 6 c. c. solution of 0.1 gm. $CaCl_2$ +normal horse serum, subcutaneously.	Dead in 27 minutes.
11061.....	475	0.23 c. c. toxine 7+1/400 c. c. antitoxic horse serum (LB 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 25 minutes later, narcosis complete, 6 c. c. solution of 0.1 gm. $CaCl_2$ +normal horse serum, subcutaneously.	Dead in 14 minutes.

TABLE NO. 6.—*Magnesium sulphate, then calcium chloride dissolved in horse serum—*
Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
11062.....	600	0.23 c. c. toxine 7+1/500 c. c. antitoxic horse serum (LB 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 24 minutes later, narcosis complete, 6 c. c. solution of 0.1 gm. $CaCl_2$ +normal horse serum, subcutaneously.	Dead in 2 hours 51 minutes.
11064.....	525	0.23 c. c. toxine 7+1/400 c. c. antitoxic horse serum (LB 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 1 hour 19 minutes later, very slight narcosis, 6 c. c. solution of 0.1 gm. $CaCl_2$ +normal horse serum, subcutaneously.	Dead in 56 minutes.
11067.....	575	0.23 c. c. toxine 7+1/500 c. c. antitoxic horse serum (LB 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 46 minutes later, narcosis complete, 6 c. c. solution of 0.1 gm. $CaCl_2$ +normal horse serum, subcutaneously.	Recovered.
11072.....	550	0.23 gm. toxine 7+1/400 c. c. antitoxic horse serum (LB 1257).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 30 minutes later, narcosis complete, 6 c. c. solution of 0.1 gm. $CaCl_2$ +normal horse serum, subcutaneously.	Dead in 90 minutes.

TABLE NO. 7.—*Magnesium sulphate, then horse serum.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10116.....	450	0.23 c. c. toxine 7+1/400 c. c. antitoxic horse serum (NYBH 10B).	92	0.35 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 55 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 65 minutes.
10115.....	450	0.23 c. c. toxine 7+1/420 c. c. antitoxic horse serum (NYBH 10B).	92	0.35 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 55 minutes later, narcosis almost complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 30 minutes.

TABLE NO. 7.—*Magnesium sulphate, then horse serum*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10106.....	425	0.23 c. c. toxine 7+1/360 c. c. antitoxic horse serum (NYBH 10B).	92	0.35 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 55 minutes later, partial narcosis, 6 c. c. normal horse serum, intraperitoneally.	Dead in 30 minutes.
10114.....	340	0.23 c. c. toxine 7+1/420 c. c. antitoxic horse serum (NYBH 10B).	92	0.35 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 55 minutes later, partial narcosis, 6 c. c. normal horse serum, intraperitoneally.	Recovered.
10117.....	400	0.23 c. c. toxine 7+1/400 c. c. antitoxic horse serum (NYBH 10B).	92	0.35 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 55 minutes later, partial narcosis, 6 c. c. normal horse serum, intraperitoneally.	Dead in 3 hours.
10029.....	450	0.23 c. c. toxine 7+1/1180 c. c. antitoxic horse serum (NYBH 310).	158	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 39 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 17 minutes.
10045.....	500	0.23 c. c. toxine 7+1/1180 c. c. antitoxic horse serum (NYBH 310).	158	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 30 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 45 minutes.
886T.....	490	0.0006 gm. toxine A+x/x c. c. antitoxic horse serum (LB).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 35 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 20 minutes.
791T.....	450	0.00006 gm. toxine A+1/250 c. c. antitoxic horse serum (PD 96E).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 60 minutes later, narcosis almost complete, 6 c. c. normal horse serum, intraperitoneally.	Recovered.
788T.....	510	0.0006 gm. toxine A+1/250 c. c. antitoxic horse serum (Mlf).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 45 minutes later, narcosis almost complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 20 minutes.

TABLE NO. 7.—*Magnesium sulphate, then horse serum*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
782T.....	570	0.0006 gm. toxine A+x/x c. c. antitoxic horse serum (LB).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 20 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Recovered.
787T.....	490	0.0006 gm. toxine A+x/x c. c. antitoxic horse serum (LB).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 31 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Dead in 18 minutes.
783T.....	550	0.0006 gm. toxine A+x/x c. c. antitoxic horse serum (LB).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 33 minutes later, narcosis complete, 6 c. c. normal horse serum, intraperitoneally.	Recovered.
785T.....	540	0.0006 gm. toxine A+x/x c. c. antitoxic horse serum (LB).	71	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 60 minutes later, partial narcosis, 6 c. c. normal horse serum, intraperitoneally.	Recovered.

TABLE NO. 8.—*Magnesium sulphate, then calcium chloride, then horse serum.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
11069.....	575	0.23 c. c. toxine 7+1/1200 c. c. antitoxic horse serum (L and B. 1245).	86	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 35 minutes later, narcosis complete, 0.1 gm. CaCl ₂ , subcutaneously. 1 minute later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 14 minutes.
11066.....	550	0.23 c. c. toxine 7+1/300 c. c. antitoxic horse serum (L. and B. 1254).	86	0.5 gm. in a 25 per cent solution of MgSO ₄ , subcutaneously. 32 minutes later, narcosis complete, 0.1 gm. CaCl ₂ , subcutaneously. 1 minute later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 38 minutes.

TABLE NO. 8.—*Magnesium sulphate, then calcium chloride, then horse serum*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
11074.....	440	0.23 c. c. toxine 7+1/600 c. c. antitoxic horse serum (L. and B. 1257).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 21 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 2 minutes later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 47 minutes.
11063.....	480	0.23 c. c. toxine 7+1/300 c. c. antitoxic horse serum (L. and B. 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 20 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 2 minutes later, 6 c. c. normal horse serum, intraperitoneally.	Recovered.
11068.....	525	0.23 c. c. toxine 7+1/500 c. c. antitoxic horse serum (L. and B. 1254).	86	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 36 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 1 minute later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 39 minutes.
10144.....	480	0.23 c. c. toxine 7+1/520 c. c. antitoxic horse serum (NYBH 13C).	88	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 27 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 2 minutes later, 6 c. c. normal horse serum, intraperitoneally.	Slight symptoms.
10126.....	570	0.23 c. c. toxine 7+1/420 c. c. antitoxic horse serum (NYBH 13C).	88	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 42 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 3 minutes later, 6 c. c. normal horse serum, intraperitoneally.	Slight symptoms.
10146.....	540	0.23 c. c. toxine 7+1/500 c. c. antitoxic horse serum (NYBH 13C).	88	0.5 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 35 minutes later, narcosis almost complete, 0.1 gm. $CaCl_2$, subcutaneously. 5 minutes later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 20 minutes.

TABLE NO. 8.—*Magnesium sulphate, then calcium chloride, then horse serum*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Results.
	<i>Grams.</i>				
10122.....	585	0.23 c. c. toxine 7+1/460 c. c. antitoxic horse serum (NYBH 13C).	88	1 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 22 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 2 minutes later, 6 c. c. normal horse serum, intraperitoneally.	No symptoms.
10145.....		0.23 c. c. toxine 7+1/520 c. c. antitoxic horse serum (NYBH 13C).	88	1 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 30 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 1 minute later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 55 minutes.
10148.....	550	0.23 c. c. toxine 7+1/600 c. c. antitoxic horse serum (NYBH 13C).	88	0.8 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 22 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 3 minutes later, 6 c. c. normal horse serum, intraperitoneally.	No symptoms.
10141.....	570	0.23 c. c. toxine 7+1/560 c. c. antitoxic horse serum (NYBH 13C).	88	0.8 gm. in a 25 per cent solution of $MgSO_4$, subcutaneously. 24 minutes later, narcosis complete, 0.1 gm. $CaCl_2$, subcutaneously. 1 minute later, 6 c. c. normal horse serum, intraperitoneally.	Dead in 15 minutes.

TABLE NO. 8a.—*Magnesium sulphate, then serum and calcium chloride.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10016.....		0.23 c. c. toxine 7+1/960 c. c. antitoxic horse serum (NYBH 310).	127	0.75 gm. in a 25 per cent solution of $MgSO_4$ subcutaneously. 30 minutes later, narcosis complete, simultaneously 6 c. c. normal horse serum intraperitoneally and 0.1 gm. 5 per cent solution of $CaCl_2$ subcutaneously.	Dead in 60 minutes.

TABLE NO. 8a.—*Magnesium sulphate, then serum and calcium chloride*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10011.....		0.23 c. c. toxine 7+1/1000 c. c. antitoxic horse serum (NYBH 310).	127	0.75 gm. in a 25 per cent solution of $MgSO_4$ subcutaneously. 35 minutes later, narcosis complete, simultaneously 6 c. c. normal horse serum intraperitoneally and 0.1 gm. 5 per cent solution of $CaCl_2$ subcutaneously.	Dead in 15 minutes.
		0.23 c. c. toxine 7+1/980 c. c. antitoxic horse serum (NYBH 310).	127	0.75 gm. in a 25 per cent solution of $MgSO_4$ subcutaneously. 37 minutes later, narcosis complete, simultaneously 6 c. c. normal horse serum intraperitoneally and 0.1 gm. 5 per cent solution of $CaCl_2$ subcutaneously.	Recovered.
10012.....	600	0.23 c. c. toxine 7+1/1000 c. c. antitoxic horse serum (NYBH 310).	127	0.75 mg. in a 25 per cent solution of $MgSO_4$ subcutaneously. 37 minutes later, narcosis complete, 6 c. c. normal horse serum intraperitoneally. 8 minutes later, 0.1 gm. of $CaCl_2$ subcutaneously.	Dead in 15 minutes.
10046.....	600	0.23 c. c. toxine 7+1/1000 c. c. antitoxic horse serum (NYBH 310).	127	0.75 mg. in a 25 per cent solution of $MgSO_4$ subcutaneously. 12 minutes later, beginning narcosis, 6 c. c. normal horse serum intraperitoneally. 9 minutes later, 0.5 gm. $CaCl_2$ subcutaneously.	Dead in 14 minutes.

TABLE NO. 9.—*Horse serum, then calcium chloride.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
	<i>Grams.</i>				
10010.....	600	0.23 c. c. toxine 7+1/1020 c. c. antitoxic horse serum (NYBH 310).	127	6 c. c. normal horse serum intraperitoneally. 5 minutes later, 0.15 gm. 5 per cent solution CaCl ₂ subcutaneously.	Dead in 15 minutes.
10008.....	600	0.23 c. c. toxine 7+1/1040 c. c. antitoxic horse serum (NYBH 310).	127	6 c. c. normal horse serum intraperitoneally. 10 minutes later, 0.1 gm. 5 per cent solution of CaCl ₂ subcutaneously.	Dead in 20 minutes.
10014.....	600	0.23 c. c. toxine 7+1/980 c. c. antitoxic horse serum (NYBH 310).	127	6 c. c. normal horse serum intraperitoneally. 5 minutes later, symptoms. 10 minutes later, 0.1 gm. 5 per cent solution of CaCl ₂ subcutaneously.	Dead in 45 minutes.

TABLE NO. 10.—*Controls, magnesium sulphate, toxic dose.*

G. P. No.	G. P. Weight.	Injection.	Result.
	<i>Grams.</i>		
Control....	415	1 gm. 25 per cent solution of MgSO ₄ subcutaneously.	Recovered.
Do.....	535	0.5 gm. 25 per cent solution of MgSO ₄ subcutaneously.	Recovered.
Do.....	420	0.6 gm. 25 per cent solution of MgSO ₄ subcutaneously. 55 minutes later, complete narcosis. 0.1 gm. 5 per cent solution of CaCl ₂ subcutaneously. Woke up 5 minutes later.	Recovered.

It is evident from the above tables that the hypnotic substances used in these experiments (urethane, paraldehyde, chloral hydrate, and magnesium sulphate) had practically no influence upon the fatal outcome of anaphylaxis. Of course, on account of the action of the hypnotic the evident symptoms of anaphylaxis were masked.

As shown by the control experiments, the amount of hypnotic used was not sufficient in itself to cause the death of the animal. While theoretically the use of such substances seemed promising, it seems from our work that they offer little or no practical advantage for this purpose.

SPECIFICITY.

In our previous papers we drew attention to the specific nature of anaphylaxis, especially when proteins of a sufficiently diverse nature are used at the first and second injections.

Gay and Southard,^a in an interesting paper on the relative specificity of anaphylaxis, report that anaphylaxis in guinea pigs caused by horse serum, egg white, or milk, is only relatively specific, and that the maximum reaction of the second injection is always obtained when the substance which has been used to sensitize is injected.

We now report further work upon the specificity of anaphylaxis in the use of horse serum, egg white, and milk, and, as will be seen from the tables, our results are not in accord with those of Gay and Southard above referred to.

In the first series (Table No. 11) 10 guinea pigs were sensitized with 1 c. c. of egg white and thirty days later were divided into three lots and tested for susceptibility to horse serum, egg white, and milk. The animals that received the horse serum and milk did not show the slightest symptoms, while the animals that received the egg white (homologous protein) died within a few minutes.

In the second series (Table No. 12), the animals received 0.01 c. c. normal horse serum at the first injection; but only those which received the homologous protein (serum) at the second injection showed any symptoms.

In the third series (Table No. 13) the animals were sensitized with 1 c. c. of milk, and only those which received the same protein at the second injection developed any symptoms.

TABLE NO. 11.—*Egg white v. horse serum and milk.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
116.....		1 c. c. saturated solution egg white subcutaneously.	30	6 c. c. normal horse (Frank) serum intraperitoneally.	No symptoms.
117.....		do.....	30	do.....	Do.
118.....		do.....	30	do.....	Do.
119.....		do.....	30	do.....	Do.
120.....		do.....	30	6 c. c. milk intraperitoneally.	Do.
121.....		do.....	30	do.....	Do.
122.....		do.....	30	do.....	Do.
123.....		do.....	30	do.....	Do.
124.....		do.....	30	do.....	Do.
125.....		do.....	30	6 c. c. egg white intraperitoneally.	Dead in 15 minutes.

^aGay, F. G., and Southard, E. E.: The relative specificity of anaphylaxis. Journ. Med. Research, vol. 19, No. 1, July, 1908, pp. 5-15.

TABLE NO. 12.—*Horse serum v. egg white and milk.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
130.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	30	6 c. c. saturated solution egg white in salt solution, intraperitoneally.	No symptoms.
132.....		do.....	30	do.....	Do.
133.....		do.....	30	do.....	Do.
135.....		do.....	30	do.....	Do.
131.....		do.....	30	6 c. c. milk, intraperitoneally.	Do.
136.....		do.....	30	do.....	Do.
137.....		do.....	30	do.....	Do.
138.....		do.....	30	do.....	Do.
139.....		do.....	30	do.....	Do.
134.....		do.....	30	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 15 minutes.

TABLE NO. 13.—*Milk v. horse serum and egg white.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
125.....		1 c. c. milk, subcutaneously.	30	6 c. c. normal horse (Frank) serum, intraperitoneally.	No symptoms.
126.....		do.....	30	do.....	Do.
127.....		do.....	30	do.....	Do.
128.....		do.....	30	do.....	Do.
129.....		do.....	30	do.....	Do.
120.....		do.....	30	6 c. c. saturated solution egg white in salt solution, intraperitoneally.	Do.
121.....		do.....	30	do.....	Do.
122.....		do.....	30	do.....	Do.
123.....		do.....	30	do.....	Do.
124.....		do.....	30	6 c. c. milk, intraperitoneally.	Severe symptoms.

Wells ^a reported experiments in which he suggests that probably the specificity of horse serum suffers somewhat after long preservation in chloroform.

We sensitized 15 guinea pigs (Table No. 14) with 0.01 c. c. anti-toxic horse serum which had been preserved under chloroform about two years, and after an interval of twenty-nine days we tested their susceptibility with egg white, milk, and normal horse serum.

The animals that had received, at the second injection, egg white and milk showed absolutely no reaction, while those receiving horse serum responded in a typical manner.

^a Wells, H. Gideon: Studies on the chemistry of anaphylaxis. Journ. Infec. Diseases, vol. 5, No. 4, October 20, 1908, pp. 449-483.

Four hours after the animals had received the injection of egg white and milk they were tested for their susceptibility to horse serum, and all responded in the usual way.

In the above experiments it is evident that the specificity of the reaction was not altered by long preservation with chloroform.

We are unable to account for the results of some other workers in regard to the specificity of the reaction, for we have invariably found that when protein substances of so different a nature as horse serum, milk, or egg white are used at the first and the second injections, the reaction is specific. In other ways we have demonstrated the specific nature of anaphylaxis.

TABLE NO. 14.—*Specificity of old serum preserved under chloroform.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
205 ^a	0.01 c. c. antitoxic horse serum (Natl. IX) preserved under chloroform about 2 years, subcutaneously.	29	6 c. c. milk, intraperitoneally.	No symptoms.
206 ^a	do.....	29	do.....	Do.
207 ^a	do.....	29	do.....	Do.
208 ^a	do.....	29	do.....	Do.
209 ^a	do.....	29	do.....	Do.
211 ^a	do.....	29	6 c. c. egg white, intraperitoneally.	Do.
212 ^a	do.....	29	do.....	Do.
213 ^a	do.....	29	do.....	Do.
214 ^a	do.....	29	do.....	Do.
215 ^a	do.....	29	do.....	Do.
Controls.					
216.....	do.....	29	4 c. c. normal horse serum, intraperitoneally.	Very severe symptoms.
217.....	do.....	29	do.....	Do.
218.....	do.....	29	do.....	Do.
219.....	do.....	29	do.....	Do.
220.....	do.....	29	do.....	Do.

^a Four hours later these animals were tested with normal horse serum and all responded in a characteristic manner.

EFFECT OF HEAT ON THE TOXICITY OF PROTEINS.

We and others have shown that the toxic action of horse serum is gradually modified by heat when the serum is in a liquid state, so that it is finally destroyed by heating at 100° C. for varying lengths of time.

Wells^a suggests, and brings forward experimental data in support, that the effect of heat in modifying or destroying the sensitizing or poisonous properties of proteins depends entirely upon its effect in

^a Wells, H. G.: Loc. cit.

rendering the proteins insoluble, rather than by the production of chemical changes in the protein.

It occurred to us that perhaps this question could be conclusively settled by first drying the proteins, then heating them to the desired temperatures, redissolving them, and testing them for their toxicity upon sensitive guinea pigs.

Dried serum can be heated to very high temperatures and subsequently redissolved with, however, a slight loss in its power of going into solution.

We dried horse serum, milk, egg white—both whole and purified egg white (the latter was kindly furnished us by Doctor Wells)—and heated them to varying degrees for different lengths of time, then redissolved them and tested the resulting solutions upon sensitive guinea pigs for toxicity.

As will be seen from the table (No. 14), heating dried serum to 130° C. for two hours or 150° C. for ten minutes, or 170° C. for ten minutes does not appreciably modify its toxicity for sensitive guinea pigs.

Likewise, egg white, both whole and purified, may be heated to 130° C. for two hours or 170° C. for ten minutes without appreciably affecting its toxicity.

Milk, when dried, may be heated to 130° C. for two hours, 150° C. for ten minutes, or 170° C. for ten minutes, and found to be apparently more toxic than we have found the unheated milk.

Likewise, whole milk may be heated to 170° C. for ten minutes or 130° C. for two hours without any apparent decrease in its toxicity.

It may be noted that when these dried proteins are heated to 130° for two hours or 170° for ten minutes they are slightly browned.

TABLE NO. 15.—*Toxicity.*

HEATED DRIED SERUM.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....	0.01 c. c. normal horse (Frank) serum, subcutaneously.	162	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 10 minutes, subcutaneously.	No symptoms.
.....	0.01 c. c. normal horse (Frank) serum, subcutaneously.	162	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 10 minutes, subcutaneously.	No symptoms.
.....	0.01 c. c. normal horse (Frank) serum, subcutaneously.	162	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 10 minutes, subcutaneously.	No symptoms.

TABLE NO. 15.—*Toxicity*—Continued.

HEATED DRIED SERUM—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
10435.....		0.245 c. c. toxine 9+1/300 c. c. antitoxic horse serum (Alex A245).	183	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 10 minutes, intraperitoneally.	Dead in 45 minutes.
10433.....		0.245 c. c. toxine 9+1/320 c. c. antitoxic horse serum (Alex A245).	183	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 10 minutes, intraperitoneally.	Dead in 60 minutes.
188.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	163	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 2 hours, intraperitoneally.	Mild symptoms.
189.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	163	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 2 hours, intraperitoneally.	Severe symptoms.
186.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	163	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 130° C. for 2 hours, intraperitoneally.	Mild symptoms.
177.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	163	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 150° C. for 10 minutes, intraperitoneally.	Very severe symptoms.
195.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	163	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 150° C. for 10 minutes, intraperitoneally.	Moderate symptoms.
198.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 170° C. for 10 minutes, intraperitoneally.	Very severe symptoms.
199.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 170° C. for 10 minutes, intraperitoneally.	Severe symptoms.
197.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	6 c. c. of 4 per cent solution of dried antitetanic horse serum heated to 170° C. for 10 minutes, intraperitoneally.	Dead in 65 minutes.

TABLE NO. 15.—*Toxicity*—Continued.

HEATED DRIED MILK.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 4 minutes.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 15 minutes.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Severe symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Very severe symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 15 minutes

TABLE No. 15.—*Toxicity*—Continued.

HEATED DRIED MILK—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....	1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Severe symptoms.
.....	1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Very severe symptoms.
.....	1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Severe symptoms.
.....	1 c. c. milk, subcutaneously.	26	6 c. c. saturated solution of dried milk heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Moderate symptoms.

HEATED DRIED EGG WHITE.

.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Moderate symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Moderate symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Mild symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 150° for 10 minutes and redissolved, intraperitoneally.	Very severe symptoms.

TABLE No. 15.—*Toxicity*—Continued.

HEATED DRIED EGG WHITE—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Very severe symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 7 minutes.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 12 minutes.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 150° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 15 minutes.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 7 minutes.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Moderate symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Moderate symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	No symptoms.
.....	1 c. c. egg white, subcutaneously.	26	6 c. c. saturated solution of dried egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	No symptoms.

HEATED PURIFIED EGG WHITE.

.....	0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
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TABLE No. 15.—*Toxicity*—Continued.

HEATED PURIFIED EGG WHITE—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Dead in 20 minutes.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Dead in 20 minutes.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 130° C. for 2 hours and redissolved, intraperitoneally.	Severe symptoms.
.....		0.01 c. c. 5 per cent solution of pure egg white subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Severe symptoms.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Severe symptoms.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution of pure egg white, subcutaneously.	21	2 c. c. of a 5 per cent solution of dried purified egg white heated to 170° C. for 10 minutes and redissolved, intraperitoneally.	Dead in 15 minutes.

TABLE No. 15.—*Toxicity*—Continued.

HEATED WHOLE MILK.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 170° C. for 10 minutes while fluid, intraperitoneally.	Dead in 14 minutes.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 170° C. for 10 minutes while fluid, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 170° C. for 10 minutes while fluid, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 170° C. for 10 minutes while fluid, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 170° C. for 10 minutes while fluid, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 130° C. for 2 hours, while fluid, intraperitoneally.	Dead in 30 minutes.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 130° C. for 2 hours, while fluid, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 130° C. for 2 hours, while fluid, intraperitoneally.	Moderate symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 130° C. for 2 hours, while fluid, intraperitoneally.	Mild symptoms.
.....		1 c. c. milk, subcutaneously.	26	6 c. c. whole milk heated to 130° C. for 2 hours, while fluid, intraperitoneally.	No symptoms.

In our first paper ^a we suggested that the sensitizing and poisoning principles in horse serum are the same, and the above results upon the toxicity of heated dried proteins tend to confirm still further this view.

^a Rosenau, M. J., and Anderson, John F.: A study of the cause of sudden death following the injection of horse serum. Hyg. Lab. Bul. 29. Washington, 1906. 95 p.

The experiments with whole milk which was heated to 170° C. for ten minutes certainly seem to show that the effect of heat depends upon the coagulability of the protein; for, as is well known, fresh milk (not acid) may be heated to high temperature without causing coagulation of any appreciable amount of the protein, whereas if undiluted serum or egg white be heated to temperatures above 60° C. they are coagulated.

We agree with Wells in believing that this is due entirely to the fact that the proteins of serum and egg white are rendered insoluble by heating, whereas those of milk are not affected.

THE EFFECT OF HEAT UPON THE SENSITIZING PROPERTY OF PROTEINS.

We and others have reported that the sensitizing property of serum is gradually affected by heating to temperatures above 80° C. until practically destroyed at 100° C. for one hour.

We now wish to report some further work on the effect of heat upon the sensitizing properties of proteins. In these experiments the various proteins used were first dried and then heated to different temperatures, subsequently redissolved, and used to sensitize guinea pigs.

As will be seen from Table No. 16, dried horse serum may be heated to 130° C. for two hours, 150° C. for ten minutes, or 170° C. for ten minutes, without impairing to any appreciable degree its sensitizing properties.

Likewise, milk may be dried, then heated to temperatures varying from 130° C. for two hours to 170° C. for ten minutes, redissolved, and found to be as potent for sensitizing as the unheated milk. Also, the fluid whole milk may be heated to 130° C. for fifteen minutes or 170° C. for ten minutes without altering its sensitizing properties.

Egg white when dried, either whole or purified, may be heated to the same high temperatures without apparently altering its ability to sensitize guinea pigs to a subsequent injection of the unheated protein.

TABLE No. 16.—*Sensitizing action.*

HEATED DRIED SERUM.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
1.....		0.01 c. c. saturated solution of dried antitetanic horse serum heated to 150° C. for 10 minutes and redissolved, subcutaneously.	6 c. c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.

TABLE NO. 16.—*Sensitizing action*—Continued.

HEATED DRIED SERUM—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
2.....		0.01 c. c. saturated solution of dried antitetanic horse serum heated to 150° C. for 10 minutes and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Dead in 12 minutes.
3.....		0.1 c. c. saturated solution of dried antitetanic horse serum heated to 150° C. for 10 minutes and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Dead in 12 minutes.
4.....		0.5 c. c. saturated solution of dried antitetanic horse serum heated to 150° C. for 10 minutes and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.
5.....		1 c. c. saturated solution of dried antitetanic horse serum heated to 150° C. for 10 minutes and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Dead in 15 minutes.
6.....		0.01 c. c. saturated solution of dried antitetanic horse serum heated to 130° C. for 2 hours and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.
7.....		0.01 c. c. saturated solution of dried antitetanic horse serum heated to 130° C. for 2 hours and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Dead in 20 minutes.
8.....		0.1 c. c. saturated solution of dried antitetanic horse serum heated to 130° C. for 2 hours and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Dead in 30 minutes.
9.....		0.5 c. c. saturated solution of dried antitetanic horse serum heated to 130° C. for 2 hours and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.
10.....		1 c. c. saturated solution of dried antitetanic horse serum heated to 130° C. for 2 hours and redissolved, subcutaneously.	27	6c.c. normal horse (Frank) serum, intraperitoneally.	Dead in 35 minutes.

TABLE No. 16.—*Sensitizing action*—Continued.

HEATED DRIED SERUM—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
11.....		0.01 c. c. saturated solution of dried antitetanic horse serum heated to 170° C. for 10 minutes and redissolved, subcutaneously.	27	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 30 minutes.
12.....		0.01 c. c. saturated solution of dried antitetanic horse serum heated to 170° C. for 10 minutes and redissolved, subcutaneously.	27	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 32 minutes.
13.....		0.1 c. c. saturated solution of dried antitetanic horse serum heated to 170° C. for 10 minutes and redissolved, subcutaneously.	27	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 35 minutes.
14.....		0.5 c. c. saturated solution of dried antitetanic horse serum heated to 170° C. for 10 minutes and redissolved, subcutaneously.	27	6 c. c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.
15.....		1 c. c. saturated solution of dried antitetanic horse serum heated to 170° C. for 10 minutes and redissolved, subcutaneously.	27	6 c. c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.

HEATED DRIED MILK.

.....		0.01 c. c. saturated solution of milk dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Severe symptoms.
.....		0.01 c. c. saturated solution of milk dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Dead in 50 minutes.
.....		0.1 c. c. saturated solution of milk dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Moderate symptoms.

TABLE No. 16.—*Sensitizing action*—Continued.

HEATED DRIED MILK—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		0.5 c. c. saturated solution of milk dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Dead in 40 minutes.
.....		1 c. c. saturated solution of milk dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Very severe symptoms.
.....		0.01 c. c. saturated solution of milk dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Severe symptoms.
.....		0.01 c. c. saturated solution of milk dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Severe symptoms.
.....		0.1 c. c. saturated solution of milk dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Severe symptoms.
.....		0.5 c. c. saturated solution of milk dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Moderate symptoms.
.....		1 c. c. saturated solution of milk dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Dead in 60 minutes.
.....		0.01 c. c. saturated solution of milk dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	No symptoms.
.....		0.01 c. c. saturated solution of milk dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	No symptoms.
.....		0.1 c. c. saturated solution of milk dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	No symptoms.

TABLE No. 16.—*Sensitizing action*—Continued.

HEATED DRIED MILK—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		0.5 c. c. saturated solution of milk dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	No symptoms.
.....		1 c. c. saturated solution of milk dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	30	6 c. c. milk intraperitoneally.	Severe symptoms.

HEATED DRIED EGG WHITE.

.....		0.01 c. c. saturated solution of egg white dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 3 minutes.
.....		0.01 c. c. saturated solution of egg white dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 15 minutes.
.....		0.1 c. c. saturated solution of egg white dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 5 minutes.
.....		0.5 c. c. saturated solution of egg white dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Mild symptoms.
.....		1 c. c. saturated solution of egg white dried and heated to 170° C. for 10 minutes and redissolved, subcutaneously.	30	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Moderate symptoms.
.....		0.01 c. c. saturated solution of egg white dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 10 minutes.

TABLE No. 16.—*Sensitizing action*—Continued.

HEATED DRIED EGG WHITE—continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....	0.01 c. c. saturated solution of egg white dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 12 minutes.
.....	0.1 c. c. saturated solution of egg white dried and heated to 150° C. for 10 minutes and redissolved subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 22 minutes.
.....	0.5 c. c. saturated solution of egg white dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 40 minutes.
.....	1 c. c. saturated solution of egg white dried and heated to 150° C. for 10 minutes and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 10 minutes.
.....	0.01 c. c. saturated solution of egg white dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Severe symptoms.
.....	0.01 c. c. saturated solution of egg white dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 5 minutes.
.....	0.1 c. c. saturated solution of egg white dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 16 minutes.
.....	0.5 c. c. saturated solution of egg white dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 15 minutes.
.....	1 c. c. saturated solution of egg white dried and heated to 130° C. for 2 hours and redissolved, subcutaneously.	34	6 c. c. saturated solution of egg white in salt solution, intraperitoneally.	Dead in 17 minutes.

TABLE No. 16.—*Sensitizing action*—Continued.

HEATED PURIFIED EGG WHITE.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 170° C. for 10 minutes and re-dissolved, subcutaneously.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 170° C. for 10 minutes and re-dissolved, subcutaneously.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 170° C. for 10 minutes and re-dissolved, subcutaneously.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 170° C. for 10 minutes and re-dissolved, subcutaneously.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 170° C. for 10 minutes and re-dissolved, subcutaneously.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 130° C. for 2 hours.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Severe symptoms.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 130° C. for 2 hours.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Severe symptoms.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 130° C. for 2 hours.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 130° C. for 2 hours.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.
.....		0.01 c. c. 5 per cent solution egg white dried and heated to 130° C. for 2 hours.	21	1 c. c. 5 per cent solution egg white, intraperitoneally.	Dead in 15 minutes.

TABLE No. 16.—*Sensitizing action*—Continued.

HEATED LIQUID MILK.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
.....		1 c. c. whole milk heated to 130° C. for 15 minutes, subcutaneously.	24	6 c. c. milk, intraperitoneally.	Severe symptoms.
.....		1 c. c. whole milk heated to 130° C. for 15 minutes, subcutaneously.	24	6 c. c. milk, intraperitoneally.	Moderate symptoms.
.....		1 c. c. whole milk heated to 130° C. for 15 minutes, subcutaneously.	24	6 c. c. milk, intraperitoneally.	Slight symptoms.
.....		1 c. c. whole milk heated to 130° C. for 15 minutes, subcutaneously.	24	6 c. c. milk, intraperitoneally.	Dead in 30 minutes.
.....		1 c. c. whole milk heated to 130° C. for 15 minutes, subcutaneously.	24	6 c. c. milk, intraperitoneally.	Moderate symptoms.
.....		1 c. c. whole milk heated to 170° C. for 10 minutes.	24	6 c. c. milk, intraperitoneally.	Slight symptoms.
.....		1 c. c. whole milk heated to 170° C. for 10 minutes.	24	6 c. c. milk, intraperitoneally.	Moderate symptoms.
.....		1 c. c. whole milk heated to 170° C. for 10 minutes.	24	6 c. c. milk, intraperitoneally.	Moderate symptoms.
.....		1 c. c. whole milk heated to 170° C. for 10 minutes.	24	6 c. c. milk, intraperitoneally.	Moderate symptoms.
.....		1 c. c. whole milk heated to 170° C. for 10 minutes.	24	6 c. c. milk, intraperitoneally.	Moderate symptoms.

In the above experiments the milk was heated to 130° for fifteen minutes in an autoclave. The liquid whole milk was brought to a temperature of 170° for ten minutes by exposing it in sealed tubes in a dry wall oven.

THE EFFECT OF HEAT UPON SENSITIVE GUINEA PIG SERUM.

Lewis has reported that the sensitizing action of sensitive guinea pig serum is apparently unaffected when heated in liquid blood to 60° for thirty minutes. In order to determine whether it is modified by higher temperatures we collected the blood from five guinea pigs which had been sensitized with a toxine-antitoxin mixture. The blood was defibrinated, centrifugalized and the serum drawn off.

Two and a half c. c. of this fresh mixed serum was injected into each of two guinea pigs, which were tested forty-eight hours later for their susceptibility and found to be sensitive.

The remainder of the serum was dried at about 37° C. An amount of this dried serum, representing 3 c. c. of the original serum, was redissolved and injected into each of two guinea pigs, which were then tested forty-eight hours later for their susceptibility and found sensitive.

The remainder of the dried serum was divided into two lots. One part was heated to 130° C. for ten minutes, the other to 100° C. for ten minutes. These two lots were then redissolved and injected into four guinea pigs, each animal receiving an amount of the dried heated serum equivalent to 3 c. c. of the fluid serum. All four guinea pigs were tested forty-eight hours later for their susceptibility. Those that received the serum heated to 130° C. for ten minutes did not show any reaction following the second injection, whereas those receiving the dried serum heated to 100° C. for ten minutes responded to the intoxicating injection.

As this serum was heated and redissolved without being pulverized some difficulty was experienced in getting it into solution, and the negative results at the higher temperature may be due in part to this fact. It is extremely interesting, however, to find that an antibody resists so high a temperature as 100° C.

SENSITIZING ACTION OF DRIED HORSE SERUM.

As a control upon the sensitizing action of heated dried serum, five guinea pigs were sensitized with varying amounts of dried tetanus antitoxin from 1/25,000 gm. to 1/800 gm. and subsequently tested by the injection of 6 c. c. of normal horse serum, intraperitoneally. All the animals were shown to be exceedingly sensitive.

TABLE No. 17.—*Sensitizing action of dried serum.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
311.....		1/25000 gm. dried tetanus antitoxin, subcutaneously.	79	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 40 minutes.
312.....		1/5000 gm. dried tetanus antitoxin, subcutaneously.	79	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 22 minutes.
313.....		1/2500 gm. dried tetanus antitoxin, subcutaneously.	79	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 20 minutes.
314.....		1/1200 gm. dried tetanus antitoxin, subcutaneously.	79	6 c. c. normal horse (Frank) serum, intraperitoneally.	Very severe symptoms.
315.....		1/800 gm. dried tetanus antitoxin, subcutaneously.	79	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 40 minutes.

SENSITIZING ACTION OF EUGLOBULINS.

Gay and Adler ^a reported that they were able to separate a substance from horse serum (euglobulins) by one-third saturation with ammonium sulphate, which was apparently a purely sensitizing substance without the admixture of a toxic or assimilable element of horse serum and which would sensitize normal animals in four or five days to a subsequent injection of horse serum.

We have previously reported ^b suggestive symptoms after four or five days in animals that had been sensitized by the injection of 0.01 c. c. of normal horse serum into the brain. Lewis reports that he has made guinea pigs quite sick on the sixth day by giving the second injection directly into the circulation.

In order to determine what amounts of euglobulins would sensitize we gave 10 guinea pigs varying amounts of euglobulins from 0.0000001 c. c. to 1 c. c. These animals were subsequently tested for their susceptibility by the injection of 6 c. c. of normal horse serum intraperitoneally. None of the animals that received smaller doses than 0.001 c. c. reacted.

We have before called attention to the fact that care must be taken in drawing conclusions as to the different effect of various agencies upon the sensitizing and toxic properties of proteins, for we have found that only 1/1,000,000 c. c. of horse serum will sensitize a guinea pig and Wells has found that 1/20,000,000 of a gram of purified egg white would do likewise. It requires considerably larger amounts to poison the animal.

TABLE NO. 18.—*Sensitizing action of euglobulins.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
109.....		0.0000001 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	No symptoms.
108.....		0.000001 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	No symptoms.
107.....		0.00001 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	No symptoms.
106.....		0.0001 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	No symptoms.

^a Gay, F. P., and Adler, H. M.: On the chemical separation of the sensitizing fraction (anaphylatin) from horse serum. Jour. Med. Research, vol. 18, June, 1908, p. 433.

^b Hyg. Lab. Bul. No. 29, 1906, p. 8.

TABLE No. 18.—*Sensitizing action of euglobulins*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
105.....		0.001 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 60 minutes.
104.....		0.01 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	Marked symptoms.
103.....		0.01 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 25 minutes.
102.....		0.01 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	No symptoms.
101.....		0.1 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	Marked symptoms.
100.....		1 c. c. euglobulins (Natl. IX), subcutaneously.	229	6 c. c. normal horse (Frank) serum, intraperitoneally.	Dead in 40 minutes.

IMMUNITY.

In order to determine whether there is any difference in the immunity conferred when the second injection is given in the brain and the immunity tested by an intraperitoneal injection, or vice versa, we took a number of sensitive guinea pigs and divided them into three lots. The first series received the second injection of serum into the brain, and the animals were tested twenty-four hours later for their immunity by intraperitoneal or subcutaneous injections.

The second series received their intoxicating injection intraperitoneally, and the animals were tested for immunity one day later, either by injections into the brain or subcutaneously.

The third series received their intoxicating dose subcutaneously and were tested one day later intraperitoneally or intracranially.

There was apparently no difference in the subsequent immunity, whether the injection was given subcutaneously, intraperitoneally, or intracranially.

TABLE No. 19.—*Immunity.*

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
176.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum intraperitoneally.	No symptoms.
146.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum intraperitoneally.	No symptoms.
172.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum intraperitoneally.	No symptoms.
174.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum intraperitoneally.	No symptoms.
149.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum, subcutaneously.	No symptoms.
173.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum, subcutaneously.	No symptoms.
175.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum, subcutaneously.	No symptoms.
170.....		0.01 c. c. normal horse serum, subcutaneously.	213	0.1 c. c. normal horse (Frank) serum, into brain; very severe symptoms. 1 day later, 6 c. c. same serum, subcutaneously.	No symptoms.
166.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	4 c. c. normal horse (Frank) serum, intraperitoneally; very severe symptoms. 1 day later, 0.2 c. c. same serum into brain.	No symptoms.

TABLE NO. 19.—*Immunity*—Continued.

G. P. No.	G. P. weight.	First injection.	Interval in days.	Second injection.	Result.
148.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	4 c. c. normal horse (Frank) serum, intraperitoneally; very severe symptoms. 1 day later, 0.2 c. c. same serum into brain.	No symptoms.
147.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	4 c. c. normal horse (Frank) serum, intraperitoneally; very severe symptoms. 1 day later, 6 c. c. same serum subcutaneously.	No symptoms.
140.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	4 c. c. normal horse (Frank) serum, intraperitoneally; very severe symptoms. 1 day later, 6 c. c. same serum subcutaneously.	No symptoms.
164.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	4 c. c. normal horse (Frank) serum, subcutaneously; severe symptoms. 1 day later, 0.2 c. c. same serum, into brain.	No symptoms.
171.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	4 c. c. normal horse (Frank) serum, subcutaneously; severe symptoms. 1 day later, 0.2 c. c. same serum, into brain.	No symptoms.
168.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	4 c. c. normal horse (Frank) serum, subcutaneously; severe symptoms. 1 day later, 6 c. c. same serum intraperitoneally.	No symptoms.
178.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	164	4 c. c. normal horse (Frank) serum, subcutaneously; severe symptoms. 1 day later, 6 c. c. same serum intraperitoneally.	No symptoms.

ANTIBODIES.

The question whether there is an antibody produced by the sensitizing injection is one that has interested all workers upon anaphylaxis. Most of them, with the exception of Gay and Southard,^a are inclined to the opinion that there is an antibody formed at the first injection.

^a Journ. Med. Research, vol. 16, 1907, p. 143.

The substance called anaphylactin, which was demonstrated by Gay and Southard, could not properly be considered as an antibody, as the sensitizing action of the transferred serum could very probably have been due to a horse serum "rest," as suggested by those authors.

However, Otto^a subsequently showed that if untreated guinea pigs be given an injection of serum of a sensitive guinea pig and tested for susceptibility twenty-four hours later, they will be found to be sensitive. This sensitizing substance, demonstrable within twenty-four hours, is very probably an antibody.

In our first paper^b we suggested, as a working hypothesis, that the first injection of the serum results in the formation of an antibody which, when brought into contact with more serum at the second injection, produces a union or reaction, resulting in the toxic manifestations.

It occurred to us that if the serum of a sensitive guinea pig be mixed with normal horse serum and its toxicity tested upon sensitive animals perhaps there might be evident an increase in the toxicity of the horse serum.

In order to test this hypothesis we bled sensitive guinea pigs which had previously received a small amount of normal horse serum. This blood was defibrinated and the serum mixed with an equal volume of normal horse serum and allowed to remain at room temperature for one hour, when the toxicity of the mixture was tested upon sensitive guinea pigs.

The blood serum of the sensitive guinea pigs used in each one of these experiments was shown by appropriate tests to contain a sensitizing substance for untreated animals.

As controls we gave sensitive guinea pigs an amount of horse serum equal to that contained in the mixture of sensitive guinea pig blood and horse serum. As further controls we also gave sensitive guinea pigs an equal amount of a mixture of normal guinea pig serum and normal horse serum, which had been allowed to remain in contact for one hour. The details of the experiments will be seen in Table No. 20.

In order to test the toxicity of such mixtures, it is necessary to determine the minimum lethal dose of horse serum, so that the control animals will receive a dose sufficient to cause symptoms in most of them, but not death; so that if there is any increase in the toxicity it will be readily manifest.

It appears from a limited amount of work, which we present in the following tables, that there was an increase in the toxicity of the

^a Munch. Med. Woch., vol. 54, 1907, p. 1665.

^b Hyg. Lab. Bul. No. 29, 1906.

horse serum due to the admixture with the serum of sensitive animals. The symptoms in those animals which had received a mixture of sensitive guinea pig and horse serum appeared much quicker and were more violent than in those animals that received the horse serum alone or the horse serum plus the normal guinea pig serum. Moreover, death occurred in a smaller percentage of the control animals.

We fully appreciate that it will require much more work upon this subject to definitely prove that the toxicity of horse serum is increased by admixture with sensitive guinea pig serum. The problem is a fundamental and important one, and is now engaging our attention. However, the limited data on hand seem sufficiently interesting and instructive to warrant publication at this time.

We have been impressed in our work upon anaphylaxis that caution must be observed in drawing conclusions from limited data because of our lack of knowledge of the fundamental principles involved, and the further fact that irregular results have occasionally been met with by almost all workers in this field.

If our further results confirm this preliminary work, it would then appear that a reaction takes place either in the animal or, more likely, in the test tube, between the blood serum of sensitive guinea pigs and the horse serum, resulting in an increase in the toxicity of the horse serum.

TABLE No. 20.—*Sensitized guinea pig serum plus normal horse serum.*

EXPERIMENT NO. 1.

G. P. No.	G. P. weight.	First injection.	Interval, in days.	Second injection.	Result.
10969.....	0.245 c. c. toxine 9+1/220 c. c. antitoxic horse serum (Alex. A245)	60	0.1 c. c. equal mixture of sensitive guinea pig and normal horse (Frank) serum, into brain.	Dead in 20 minutes.
10695.....	0.245 c. c. toxine 9+1/240 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of sensitive guinea pig and normal horse (Frank) serum, into brain.	Dead in 3 minutes.
10995.....	0.245 c. c. toxine 9+1/500 c. c. antitoxic horse serum (Alex. A249).	60	0.1 c. c. equal mixture of sensitive guinea pig and normal horse (Frank) serum, into brain.	Dead in 4 minutes.
10978.....	0.245 c. c. toxine 9+1/270 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of sensitive guinea pig and normal horse (Frank) serum, into brain.	Dead in 4 minutes.
11018.....	0.245 c. c. toxine 9+1/640 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of sensitive guinea pig and normal horse (Frank) serum, into brain.	Dead in 4 minutes.

TABLE NO. 20.—*Sensitized guinea pig serum plus normal horse serum*—Continued.

EXPERIMENT NO. 1—continued.

G. P. No.	G. P. weight.	First injection.	Interval, in days.	Second injection.	Result.
11016.....		0.245 c. c. toxine 9+1/660 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of sensitive guinea pig and normal horse (Frank) serum, into brain.	Dead in 6 minutes.
Controls.					
10994.....		0.245 c. c. toxine 9+1/520 c. c. antitoxic horse serum (Alex. A249).	60	0.1 c. c. equal mixture of normal guinea pig and normal horse serum, into brain.	Severe symptoms.
10017.....		0.245 c. c. toxine 9+1/640 c. c. antitoxic horse serum (Alex. A249).	60	0.1 c. c. equal mixture of normal guinea pig and normal horse serum, into brain.	Very severe symptoms.
10990.....		0.245 c. c. toxine 9+1/320 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of normal guinea pig and normal horse serum, into brain.	Dead in 12 minutes.
10970.....		0.245 c. c. toxine 9+1/220 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of normal guinea pig and normal horse serum, into brain.	Severe symptoms.
10989.....		0.245 c. c. toxine 9+1/320 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of normal guinea pig and normal horse serum, into brain.	Dead in 11 minutes.
10987.....		0.245 c. c. toxine 9+1/330 c. c. antitoxic horse serum (Alex. A245).	60	0.1 c. c. equal mixture of normal guinea pig and normal horse serum, into brain.	Very severe symptoms.

EXPERIMENT NO. 2.

111.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Severe symptoms.
112.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Very severe symptoms.
113.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Severe symptoms.
114.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Very severe symptoms.
115.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Severe symptoms.

TABLE NO. 20.—*Sensitized guinea pig serum plus normal horse serum*—Continued.

EXPERIMENT NO. 2—continued.

G. P. No.	G. P. weight.	First injection.	Interval, in days.	Second injection.	Result.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.05 c. c. normal horse (Frank) serum, into brain.	No symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.05 c. c. normal horse (Frank) serum, into brain.	No symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.05 c. c. normal horse (Frank) serum, into brain.	No symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.05 c. c. normal horse (Frank) serum, into brain.	Mild symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.05 c. c. normal horse (Frank) serum, into brain.	Marked symptoms.

EXPERIMENT NO. 3.

10910.....		0.245 c. c. toxine 9+1/600 c. c. antitoxic horse serum (NYBH 306).	94	0.1 c. c. equal amount of sensitive guinea-pig and normal horse serum, into brain.	Dead in 6 minutes.
10960.....		0.245 c. c. toxine 9+1/420 c. c. antitoxic horse serum (PD 07635).	94	0.1 c. c. equal amount of sensitive guinea-pig and normal horse serum, into brain.	Dead in 5 minutes.
10829.....		0.245 c. c. toxine 9+1/900 c. c. antitoxic horse serum (NYBH 305).	100	0.1 c. c. equal amount of sensitive guinea-pig and normal horse serum, into brain.	Dead in 6 minutes.
10815.....		0.245 c. c. toxine 9+1/740 c. c. antitoxic horse serum (NYBH 305).	100	0.1 c. c. equal amount of sensitive guinea-pig and normal horse serum, into brain.	Dead in 35 minutes.
10833.....		0.245 c. c. toxine 9+1/1080 c. c. antitoxic horse serum (NYBH 305).	100	0.1 c. c. equal amount of sensitive guinea-pig and normal horse serum, into brain.	Dead in 5 minutes.
Control.....		0.245 c. c. toxine 9+1/600 c. c. antitoxic horse serum (NYBH).	94	0.05 c. c. normal horse (Frank) serum, into brain.	Severe symptoms.
Control.....		0.245 c. c. toxine 42+1/700 c. c. antitoxic horse serum (NYBH 305).	100	0.05 c. c. normal horse (Frank) serum, into brain.	Severe symptoms.
Control.....		0.245 c. c. toxine 42+1/940 c. c. antitoxic horse serum (NYBH 305).	100	0.05 c. c. normal horse (Frank) serum, into brain.	Very severe symptoms.
Control.....		0.245 c. c. toxine 42+1/1020 c. c. antitoxic horse serum (NYBH 305).	100	0.05 c. c. normal horse (Frank) serum, into brain.	Very severe symptoms.

TABLE NO. 20.—*Sensitized guinea pig serum plus normal horse serum*—Continued.

EXPERIMENT NO. 4.

G. P. No.	G. P. weight.	First injection.	Interval, in days.	Second injection.	Result.
101.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.2 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Very severe symptoms.
102.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.2 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Dead in 4 minutes.
103.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.2 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Very severe symptoms.
104.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.2 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Very severe symptoms.
105.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.2 c. c. equal mixture of sensitive guinea-pig serum and normal horse serum, into brain.	Very severe symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. normal horse (Frank) serum, into brain.	Marked symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. normal horse (Frank) serum, into brain.	Marked symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. normal horse (Frank) serum, into brain.	Severe symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. normal horse (Frank) serum, into brain.	Severe symptoms.
Control.....		0.01 c. c. normal horse (Frank) serum, subcutaneously.	56	0.1 c. c. normal horse (Frank) serum, into brain.	Marked symptoms.

TIME.

The longest interval that has elapsed between the first and the second injection of serum in guinea pigs in our work previously reported has been seven hundred and thirty-two days. We have recently, however, tested the susceptibility of a guinea pig that had received the first injection of serum one thousand and ninety-six days (a little over three years) before it was tested for its susceptibility. This animal was found to be still extremely sensitive. We believe that sensitive guinea pigs retain their susceptibility during their entire life.

SUMMARY AND CONCLUSIONS.

While the use of hypnotics appeared promising for the prevention of anaphylaxis, it seems, from our work, that they offer little or no practical advantage for this purpose. We used in our experiments urethane, paraldehyde, chloral hydrate, and magnesium sulphate. These substances have practically no influence upon the fatal outcome of anaphylaxis.

Further work upon the specificity of anaphylaxis emphasizes the specific nature of this phenomenon.

The effect of heat in modifying or destroying the sensitizing or poisonous properties of proteins probably depends entirely upon its effect in rendering the proteins insoluble, rather than by the production of chemical changes in the protein.

It was found that heating dried horse serum to 130°C . for two hours or 150°C . for ten minutes or 170°C . for ten minutes did not appreciably modify its toxicity for sensitive guinea pigs.

Dried egg white, whether whole or purified, may be heated to 130°C . for two hours or 170°C . for ten minutes without appreciably affecting its toxicity for sensitive guinea pigs.

Milk when dried may be heated to 130°C . for two hours, 150°C . for ten minutes, or 170°C . for ten minutes, and found to be apparently more toxic than the unheated serum. Whole fluid milk may be heated to 170°C . for ten minutes or 130°C . for two hours without any apparent decrease in its toxicity.

Dried horse serum may be heated to 130°C . for two hours, 150°C . for ten minutes, or 170°C . for ten minutes, without impairing to any appreciable degree its sensitizing properties.

Dried milk may be heated to temperatures varying from 130°C . for two hours to 170°C . for ten minutes and redissolved, and found to be as potent for sensitizing as unheated milk.

Fluid milk may be heated to 130°C . for fifteen minutes or 170°C . for ten minutes without altering its sensitizing properties.

Dried egg white, either whole or purified, may be heated to the same high temperatures without apparently altering its ability to sensitize guinea pigs.

The sensitizing substance in sensitive guinea pig serum, when dried, may be heated to at least 100°C . for ten minutes without destroying its power to sensitize guinea pigs within forty-eight hours.

Animals sensitized with euglobulins prepared by one-third saturation with ammonium sulphate were not sensitive when amounts smaller than 0.001 c. c. were used, while amounts larger than this sensitized guinea pigs.

There is apparently no difference in the subsequent immunity whether the intoxicating injection be given subcutaneously, intraperitoneally, or intracranially. In these cases the immunity was tested twenty-four hours after the second injection.

We present preliminary evidence suggesting that antibodies are concerned in the mechanism of anaphylaxis. The mixture of normal horse serum with the blood serum of a sensitive guinea pig apparently increases the toxicity of the horse serum for sensitive guinea pigs.

We have shown that guinea pigs may remain sensitive one thousand and ninety-six days; that is, a little over three years.

LIST OF HYGIENIC LABORATORY BULLETINS OF THE PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.

The Hygienic Laboratory was established in New York, at the Marine Hospital on Staten Island, August, 1887. It was transferred to Washington, with quarters in the Butler Building, June 11, 1891, and a new laboratory building, located in Washington, was authorized by act of Congress, March 3, 1901.

The following *bulletins* [Bulls. Nos. 1-7, 1900 to 1902, Hyg. Lab., U. S. Mar.-Hosp. Serv., Wash.] have been issued:

*No. 1.—Preliminary note on the viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 2.—Formalin disinfection of baggage without apparatus. By M. J. Rosenau.

*No. 3.—Sulphur dioxide as a germicidal agent. By H. D. Geddings.

*No. 4.—Viability of the *Bacillus pestis*. By M. J. Rosenau.

No. 5.—An investigation of a pathogenic microbe (*B. typhi murium* Danyz) applied to the destruction of rats. By M. J. Rosenau.

*No. 6.—Disinfection against mosquitoes with formaldehyde and sulphur dioxide. By M. J. Rosenau.

No. 7.—Laboratory technique: Ring test for indol, by S. B. Grubbs and Edward Francis; Colloidal sacs, by S. B. Grubbs and Edward Francis; Microphotography with simple apparatus, by H. B. Parker.

By act of Congress approved July 1, 1902, the name of the "United States Marine-Hospital Service" was changed to the "Public Health and Marine-Hospital Service of the United States," and three new divisions were added to the Hygienic Laboratory.

Since the change of name of the Service the bulletins of the Hygienic Laboratory have been continued in the same numerical order, as follows:

*No. 8.—Laboratory course in pathology and bacteriology. By M. J. Rosenau. (Revised edition, March, 1904.)

*No. 9.—Presence of tetanus in commercial gelatin. By John F. Anderson.

No. 10.—Report upon the prevalence and geographic distribution of hookworm disease (uncinariasis or ancylostomiasis) in the United States. By Ch. Wardell Stiles.

*No. 11.—An experimental investigation of *Trypanosoma lewisi*. By Edward Francis.

*No. 12.—The bacteriological impurities of vaccine virus; an experimental study. By M. J. Rosenau.

*No. 13.—A statistical study of the intestinal parasites of 500 white male patients at the United States Government Hospital for the Insane; by Philip E. Garrison, Brayton H. Ransom, and Earle C. Stevenson. A parasitic roundworm (*Agamomermis culicis* n. g., n. sp.) in American mosquitoes (*Culex sollicitans*); by Ch. Wardell Stiles. The type species of the cestode genus *Hymenolepis*; by Ch. Wardell Stiles.

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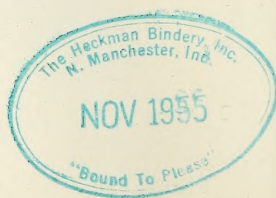
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